Radiation Oncology

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Annual Scientific Meeting

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Drury Plaza Riverwalk Hotel

San Antonio
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Saturday, October 17, 2015

8:00 – 9:00 AM VRTOG Meeting Medina Room

9:00 – 10:00 AM ACVR KEYNOTE ADDRESS Medina Room
Dr. Eric Hall
Higgins Professor Emeritus of Radiation Biophysics
Special Lecturer in Radiation Oncology
Center for Radiological Research
College of Physicians and Surgeons
Columbia University

9:00 – 10:00 AM ACVR KEYNOTE ADDRESS Medina Room

10:00 – 10:30 AM BREAK

10:30 AM – 12:00 PM SCIENTIFIC SESSION 1 Medina Room

10:30 – 10:45 AM A RETROSPECTIVE ANALYSIS OF MULTIMODALITY TREATMENT FOR CANINE ORAL MELANOMA: 126 CASES. M. Turek, T. LaDue, J. Looper, K. Nagata, K. Shiomitsu, M. Keyerleber, J. Buchholz, T. Gieger, D. Vail. University of Wisconsin-Madison School of Veterinary Medicine, Madison, WI, 53706

10:45 – 11:00 AM GRID THERAPY FOR SPONTANEOUSLY- OCCURRING, MACROSCOPIC SOFT TISSUE SARCOMAS IN DOGS M.W. Nolan, T.L. Gieger, L.P. Posner, J.N. Rivera, D.M. Roback, S.X. Chang. College of Veterinary Medicine, North Carolina State University, NC, 27607

11:00AM – 11:15 AM HIGH DOSE SINGLE FRACTION RADIATION THERAPY FOR PRESUMED CARDIAC HEMANGIOSARCOMA IN PET DOGS M.W. Nolan, M.M. Arkans, D. LaVine, E. Griffith, T. DeFrancesco, L.P. Posner, B. Keene, S. Tou, T.L. Gieger 1- College of Veterinary Medicine, North Carolina State University, NC, 27607.

11:15 - 11:30 AM SURVEY OF IMRT TARGET DESIGN AND NORMAL TISSUE DELINEATION IN CANINE NASAL TUMOR RADIATION TREATMENT PLANNING M. Turek, M. Henzler, N. Christensen, L. Forrest. University of Wisconsin-Madison School of Veterinary Medicine, WI, 53706
11:30 – 11:45 AM  COMPARISON OF A PALLIATIVE CYCLICAL RADIOTHERAPY REGIMEN (‘QUAD-SHOT’) WITH HYPOFRACTIONATION IN 65 DOGS WITH ADVANCED SINONASAL TUMOURS. DESCRIPTION OF A NOVEL VOLUMETRIC SCORING AND RISK INDEX  J. Benoit, B. Balañá, A. Petite, F.J. López


12:00 PM – 1:30 PM  RADIATION ONCOLOGY BUSINESS MEETING LUNCH

1:30 – 3:00 PM  SCIENTIFIC SESSION 2

1:30 – 1:45 PM  STEREOTACTIC RADIOSURGERY FOR TREATMENT OF FELINE NASAL LYMPHOMA WITH OR WITHOUT ADJUVANT CHEMOTHERAPY. K.E. Pohlmann, J.T. Custis, S.M. LaRue. Colorado State University, Colorado 80523

1:45 – 2:00 PM  DOSIMETRY OF CONTINUOUS MOTION IN STRONTIUM–90 PLESIOTHERAPY. J.R. Schutte, J.C. Lattimer, K. A. Selting, C. A. Maitz. University of Missouri Veterinary Medical Teaching Hospital, Missouri, 65211.

2:00 – 2:15 PM  OUTCOME OF 9 DOGS TREATED WITH STEREOTACTIC RADIATION THERAPY FOR VERTEBRAL OSTEOSARCOMA Swift, K., Custis, J., LaRue S. Colorado State University, Fort Collins CO 80534


2:30 – 2:45 PM  GLYCOLYTIC PHENOTYPING OF CANINE MAST CELL TUMORS L.R. Griffin, D. Thamm, E. Ehrhart, A. Marolf, E. Randall
2:45 – 3:00 PM  EXPRESSION OF COX–2 AND NAG–1 IN CANINE INTRANASAL CARCINOMA  M. M. Parys, P. W. Snyder, H. Y. Weng, A. K. Clark, D. W. Knapp, G. C. Lantz, J. M. Poulson. Purdue University, College of Veterinary Medicine, West Lafayette, Indiana, 47907, United States

3:00 – 3:30 PM  BREAK

3:30 – 5:00 PM  GROUP DISCUSSION  Medina Room
A RETROSPECTIVE ANALYSIS OF MULTIMODALITY TREATMENT FOR CANINE ORAL MELANOMA: 126 CASES

M. Turek¹, T. LaDue², J. Looper³, K. Nagata⁴, K. Shiomitsu⁵, M. Keyerleber⁶, J. Buchholz⁷, T. Gieger⁵, D. Vail¹. ¹University of Wisconsin-Madison School of Veterinary Medicine, WI, 53706; ²SE Veterinary Oncology and Internal Medicine, FL 32073; ³VCA Aurora Animal Hospital, IL 60506 and Chicago Veterinary Cancer Center, IL 60618; ⁴University of Georgia College of Veterinary Medicine, GA 30602; ⁵Louisiana State University School of Veterinary Medicine, LA 70803; ⁶Tufts University Cummings School of Veterinary Medicine, MA 01536; ⁷Animal Oncology and Imaging Center, Switzerland

Introduction/Purpose: Oral melanoma (OM) has a high propensity to metastasize to regional lymph nodes (LN) and lungs. Surgery and/or radiotherapy (RT) are effective local treatments, however most dogs succumb to distant metastasis. Immunotherapy represents an attractive strategy for this potentially immunogenic tumor type. The objective of this multi-institutional retrospective study was to examine the clinical outcome of dogs with OM treated with ONCEPT™ melanoma vaccine, +/- surgery and/or RT. This is a VRTOG collaboration.

Methods: Medical records of dogs with OM treated with ONCEPT™ were reviewed from seven VRTOG institutions. Many dogs underwent concurrent surgery and/or RT (8 Gray X 4 weekly fractions). Dogs with distant metastasis and those receiving concurrent chemotherapy were excluded.

Results: One hundred and twenty six dogs were included. All received ONCEPT™. Sixty had adequate local control (ALC; complete excision or irradiation of microscopic disease). Fifteen were treated in the microscopic setting. Fifty-one were treated in the gross disease setting, of which 39 underwent RT. Median time to progression, median progression-free survival and median overall survival were 304, 244 and 617 days, respectively. Dogs with ALC had improved clinical outcomes. The following also correlated with favorable clinical outcomes: rostral location, stage 1, absence of LN metastasis, low mitotic index, absence of bony lysis, absence of gross disease.

Discussion/Conclusion: This is the largest reported series of dogs with OM treated with ONCEPT™. Clinical outcomes are similar to those reported recently for dogs treated with surgery and/or RT alone. Several prognostic indicators were confirmed. A prospective, randomized, controlled study is needed to determine the clinical benefit of ONCEPT™.
GRID THERAPY FOR SPONTANEOUSLY-OCCURRING, MACROSCOPIC SOFT TISSUE SARCOMAS IN DOGS

M.W. Nolan¹,³, T.L. Gieger¹,³, L.P. Posner², J.N. Rivera⁵, D.M. Roback⁴, S.X. Chang¹,⁵ 1- Dept of Clinical Sciences; 2- Dept of Molecular Biomedical Sciences; 3- Center for Comparative Medicine and Translational Research, College of Veterinary Medicine, North Carolina State University, NC, 27607; 4- Rex Cancer Center, Raleigh, NC 27607; 5- Dept of Radiation Oncology, University of North Carolina, Chapel Hill, NC 27514

Introduction/Purpose: Spatially-fractionated radiation therapy (SFRT) intentionally directs alternating regions of high and low dose at tumors. When combined with conventional full-course radiation therapy, clinical reports suggest that SFRT (in the form of GRID therapy) can result in impressive cytoreduction of bulky tumors in human patients; used alone, GRID is reportedly ineffective in people. Rodent studies, using mini- and microbeam irradiation, provide evidence that SFRT has a high therapeutic ratio, which may be facilitated via induction of unique microenvironmental changes. However, the mechanism(s) by which SFRT induce such encouraging clinical responses remains unclear. Rational clinical implementation requires clarification of the physical and biological attributes of SFRT. A large animal model that complements existing rodent systems is needed. This study characterizes the response of pet dogs with naturally-occurring soft tissue sarcoma (STS) to GRID therapy, to (1) determine the feasibility of using these animals as a clinically relevant model for studying responses to SFRT in human cancer patients, and (2) to assess the potential for using such therapy as a means of delivering palliative-intent therapy to canine sarcoma patients.

Methods: A prospective pilot study was undertaken, including STS that were at least 6 cm diameter. A CT-based GRID therapy plan was generated for each subject, wherein a single fraction of 20 or 25 Gy was prescribed to Dmax, using a 6 MV photon beam and GRID collimator. Acute toxicity was assessed 2, 4 and 6 weeks after irradiation. Wash-in kinetics of intravenously-administered iodinated contrast media were assessed at baseline and again 6 weeks after treatment. Serum vascular endothelial growth factor (VEGF) was assayed at baseline, 1, 4, 24 and 48 hours after GRID irradiation.

Results: Six dogs were treated with GRID alone, at 20 Gy (3 dogs) and 25 Gy (3 dogs). None experienced a measurable response, per RECIST. Acute RTOG grade I skin toxicity was observed in 3/6 dogs, with 2/3 having received 25 Gy GRID. There was a trend towards platelet-corrected serum VEGF concentration being lower 1 and 48 hours after GRID, than at baseline. There were no observed differences in wash-in kinetics.

Discussion/Conclusion: Canine responses to GRID mirror those of humans, in that there was evidence of tumor microenvironment alteration shortly after treatment, and no measurable tumor response to GRID alone. While GRID alone will not be a useful palliative measure for sarcomas, the clinical utility of SFRT may be improved if combined with conventional therapy.
HIGH DOSE SINGLE FRACTION RADIATION THERAPY FOR PRESUMED CARDIAC HEMANGIOSARCOMA IN PET DOGS
M.W. Nolan¹, M.M. Arkans¹, D. LaVine¹, E. Griffith³, T. DeFrancesco¹, L.P. Posner², B. Keene¹, S. Tou¹, T.L. Gieger¹, 1- Department of Clinical Sciences; 2- Department of Molecular Biomedical Sciences; 3- Department of Statistics; 4- Center for Comparative Medicine and Translational Research, College of Veterinary Medicine, North Carolina State University, NC, 27607.

Introduction/Purpose: Cardiac hemangiosarcoma (cHSA) is a malignant tumor of vascular origin, typically arising on the right atrium or auricular appendage. Though the metastatic potential is high, without intervention, most dogs succumb to recurrent pericardial effusion (median survival time of 12 days). The best reported outcomes have been achieved with a combination of surgical resection and chemotherapy (median survival time ~6 months). However, tumor location and extent, surgical risks (morbidity and mortality), prognosis and financial constraints often preclude surgery. The purpose of this study was to determine if high dose, single fraction radiation therapy (HD-SFRT) reduces frequency of pericardial effusion, or prolongs survival in dogs with a clinical diagnosis of cHSA.

Methods: A prospective pilot study was performed, wherein dogs with echocardiographic evidence of a right atrial/auricular mass and hemorrhagic pericardial effusion were treated with single fraction of 12 Gy, delivered using conventional irradiation techniques (a CT-based, computerized treatment planning was utilized to generate a radiation plan constructed with MLC-shaped, parallel-opposed 6 MV photon beams). Serum troponin and ceramide levels, and plasma concentrations of vascular endothelial growth factor (VEGF) were quantified before, 4 and 24 hours after HD-SFRT. The incidence of cardiac tamponade (quantified as the number of pericardiocenteses per 2 week period) before HD-SFRT was compared to that after treatment. Overall survival time was determined. Several potential predictive and/or prognostic biomarkers were evaluated.

Results: Six dogs were treated with HD-SFRT for presumed cHSA. Median survival time (from the time of irradiation) was 79 days (range: 35 to 136 days). The frequency of required pericardiocenteses decreased after treatment (p=0.03). Pre- and post-treatment plasma VEGF concentrations (n=5) were not statistically significantly different at any timepoint. Histopathology confirmed cardiac hemangiosarcoma in 4/5 dogs for which results of post-mortem examination were available. Of note, 2/6 dogs were treated with carboplatin chemotherapy, after both HD-SFRT and sample collection.

Discussion/Conclusion: HD-SFRT is an attractive alternative to surgery for local control of cHSA in dogs. In this population of dogs, SFRT appeared safe, and reduced the frequency of recurrent pericardial effusion and tamponade. Radiation dose escalation and/or combination with chemotherapy may further improve outcomes.
SURVEY OF IMRT TARGET DESIGN AND NORMAL TISSUE DELINEATION IN CANINE NASAL TUMOR RADIATION TREATMENT PLANNING
M. Turek¹, M. Henzler, N. Christensen, L. Forrest. University of Wisconsin-Madison School of Veterinary Medicine, WI, 53706

Introduction/Purpose: Anatomy and tumor target delineation are critical components of treatment planning. The development of conformal radiotherapy with its expected therapeutic gain, as well as the increased risk of geographic misses, requires accurate definition of margins around tumor volumes. In veterinary medicine, contouring guidelines do not exist. Variability in contouring presents challenges for comparative analysis of the literature, repeatability of clinical outcomes, as well as for consistency in clinical trials. The objective of this study was to assess inter-clinician contouring and clinical practices in order to bring awareness to the need for standardization. Our hypothesis is that heterogeneity exists among veterinary radiation oncologists in IMRT target design, normal tissue delineation and clinical practice.

Methods: Veterinary radiation oncologists with access to IMRT were provided common CT data sets from 2 dogs with sinonasal carcinoma (one stage II case and one stage IV case) and completed a questionnaire to identify variables affecting contouring practices. Participants were asked to contour the tumor targets as well as organs at risk (OAR) according to their standard definitive-intent IMRT planning practices. Contoured CT data sets were analyzed anonymously using StructSure™ software designed to quantitatively compare contour volumes. Structures were analyzed for agreement and volume overlap using a metric score and dice similarity coefficient, respectively.

Results: Nine of 13 solicited radiation oncologists responded to the survey. IMRT techniques included dynamic (6), step and shoot (2) and tomotherapy (1). For both data sets, structures contoured by all participants included PTV, OS, OD and brain. Multiple other OAR were contoured by 1 to 6 participants. There was disparity in the use of PTV. Greater contouring variation occurred for target structures than for OAR. CTV was associated with the greatest inconsistency in overlap and had the largest penalty for disagreement between participants. CTV disparity was seen in inclusion of the lesser-affected nasal cavity, the nasopharynx, the soft tissues (stage IV case) and the frontal sinuses. GTV and CTV variation occurred when fluid was contoured. Best agreement occurred for brain and lenses. Variation in ocular contours occurred at rostral and caudal borders. Dose prescription was ≥51Gy to the PTV for all participants. Two participants pursued elective local nodal irradiation. Four indicated that adjuvant medical therapy would be offered.

Discussion/Conclusion: This study demonstrates heterogeneity in nasal tumor IMRT contouring practices. Efforts to standardize definitions and techniques are desirable to optimize analysis and repeatability of reported clinical outcomes.
COMPARISON OF A PALLIATIVE CYCLICAL RADIOtherapy REGIMEN (‘QUAD-SHOT’) WITH HYPOFRACTIONATION IN 65 DOGS WITH ADVANCED SINONASAL TUMOURS. DESCRIPTION OF A NOVEL VOLUMETRIC SCORING AND RISK INDEX.
J. Boizot, B. Balañá, A. Petite, F.J. López

Introduction/Purpose: Advanced sinonasal tumours in dogs are frequently treated palliatively due to their poor prognosis. Survival times beyond one year may be achieved however with the use of hypofractionated, palliative radiation therapy. Alternative protocols might further improve prognosis for dogs with advanced stage disease. In this study, the aims were to compare the efficacy and toxicity of a palliative high total dose, fractionated, cyclical regimen (‘Quad-Shot’) with a standard hypofractionated protocol. Prognostic factors, including the use of a novel CT-based volumetric score; and a risk index system were also evaluated.

Methods: Records of canine patients with histologically confirmed, CT stage 3-4 sinonasal tumours, treated palliatively at a private referral hospital (2006-2013) with either a hypofractionated (HF) or a cyclical radiotherapy course (QS), were reviewed. Exclusion criteria included round cell tumours, melanomas or nasal planum tumours. All CT images were reviewed by a board certified radiologist blinded to the case description. A CT-based volumetric score (VS) was developed based on the number of Adams criteria was developed. Dogs treated with the QS protocol received 4Gy twice daily on 2 consecutive days (16Gy) every 3 to 4 weeks for a total of 3 cycles (48Gy). Dogs treated with the HF protocol received 32-36Gy as 4 to 6 once weekly fractions. Survival times were analysed using the Kaplan-Meier method and prognostic factors for survival and a risk index were evaluated by multivariate Cox-regression analysis. P-values <.05 were considered statistically significant.

Results: 65 dogs met inclusion criteria (Group 1, HF (n=43); Group 2, QS (n=22)). Groups were statistically similar (age, duration of signs, CT stage, VS and tumour types). The MST for group 2 (404d (95% CI 251-556d)) was significantly longer than for group 1 (MST 185d (95% CI 105-269d) (p=.015)). Negative prognostic factors for survival were treatment with a HF protocol, age >10 years (p=.003), clinical signs for <3 months (p=.002), lysis of frontal sinus / calvarium (p=.001) and VS>4 (p=.001). High-risk patients (index>2 negative factors) had a significantly shorter MST (152d; 95% CI 117-187d) compared to low-risk patients (452d; 95% CI 353 - 550d) (p=.000). The index was highly correlated with survival. CT stage was not associated with MST. The occurrence of grade 2 and grade 3 acute (Group 1, 83% vs. Group 2, 27%) and delayed radiation side effects (Group 1, 49% vs. Group 2, 23%) were significantly higher in dogs receiving a HF protocol with p-values of .000034 and .036 respectively.

Discussion/Conclusion: The cyclical regimen was well tolerated and was associated with longer MST compared to HF radiotherapy for the treatment of advanced canine sinonasal tumours. The VS and risk index predicted prognosis more effectively than the Adams modified staging system. Future studies may include the use of the cyclical regimen for treatment of early stage sinonasal tumours when pet owners decline definitive radiation therapy.
ASSESSMENT OF ISOCENTER PLACEMENT AND TUMOR VOLUME BY MULTIPLE OPERATORS.

Purpose: To evaluate isocenter placement and tumor volume as determined by different operators. Little variation was expected within an individual operator's assessments. Greater variation was expected between individual operators.

Methods: A CT scan of a single canine brain tumor was evaluated by several operators who were instructed to contour only the tumor. Contouring parameters were the same for all operators. Multiple contouring sessions were performed by each operator who was unaware of the results. Isocenters and volumes were calculated on an ADAC Pinnacle3 therapy planning computer. Isocenter coordinates (x, y, z) were assessed as ranges and averages within an individual’s work and between individuals. This process was also performed for assessment of tumor volumes.

Results: Contrary to expectation, there was little variability in isocenter placement as determined by x, y, z coordinates within and between operators. Tumor volume varied with individual operators’ average volumes ranging from 4.31 cm³ below (18.6 %) to 5.90 cm³ (10.4%) above the average volume of 5.29 cm³ for all contours. Variation between the smallest and largest individual tumor volumes was 34.8%. Variation in tumor volume ranged from 5.4% to 32% within individual operator’s assessments.

Conclusion: Isocenter placement is less variable between operators than expected. Tumor volume has greater variation, both within an individual operator’s plans and between operators with the potential for large differences between dose to tumor and normal tissue. Efforts to precisely replicate isocenter for therapy may be for naught if there is little agreement about tumor volume. Further evaluation of tumor contouring protocols should be a priority for future research.
STEREOTACTIC RADIOSURGERY FOR TREATMENT OF FELINE NASAL LYMPHOMA WITH OR WITHOUT ADJUVANT CHEMOTHERAPY.
K.E. Pohlmann, J.T. Custis, S.M. LaRue. Flint Animal Cancer Center, Department of Environmental and Radiological Health Sciences, Colorado State University, Colorado 80523

Introduction/Purpose: Nasal lymphoma represents the most commonly diagnosed nasal tumor in cats. The majority of patients present with localized disease, however involvement of regional lymph nodes and distant organs has been reported. Common treatments include fractionated radiation therapy and/or chemotherapy. Lymphoid neoplasms are exceptionally radiosensitive and fractionated radiation therapy has provided good long-term local tumor control. Typical fractionated protocols require repeated anesthetic events, which may be contraindicated based on concomitant conditions. For such patients, expedited protocols are preferred. Stereotactic radiosurgery (SRS) is an extremely focused form of radiation that allows treatment to be administered in a single fraction while remaining within normal tissue tolerance. The purpose of this ongoing study is to evaluate the outcomes of patients with nasal lymphoma treated with SRS with or without adjuvant chemotherapy.

Methods: Feline patients diagnosed with nasal lymphoma from June 2014 to the present who presented to the CSU VTH for radiation therapy were evaluated for inclusion in this study. Medical histories were reviewed to extract information on patient demographics, oncological history, clinical signs related to nasal disease, previous diagnostics, and previous treatment. All patients underwent staging to include complete blood count, serum biochemistry, thoracic radiographs, radiation planning CT of the skull, and cytology of palpably enlarged lymph nodes when possible. For inclusion cats had to have a histopathologic diagnosis of nasal lymphoma and undergo stereotactic radiation prescribed at 20 Gray delivered in a single fraction. Regional lymph nodes were irradiated in patients in which involvement was confirmed by cytology or suspected based on CT. Survival parameters were determined using Kaplan-Meier analysis. Toxicity was graded according to the criteria defined by the Veterinary Radiation Therapy and Oncology group.

Results: Seven cats met the criteria for inclusion in the study. There were two domestic shorthairs and one domestic longhair, domestic medium hair, Maine Coon, Oriental Shorthair, and Egyptian mix. There were three castrated males and four spayed females. The median age of patients was 10.8 years. Histopathological diagnosis of lymphoma was confirmed in all patients. Two patients received radiation treatment for their nasal disease only. In five patients, the regional lymph nodes were included in the treatment field. Cytology confirmed metastasis in only one patient; in four patients lymph nodes were enlarged on CT and cytology could not confirm or rule out metastasis. All patients were treated with prednisolone. Three patients received chemotherapy following radiation. At the time of analysis all patients were alive. Median follow-up time was 314 days. No patients had evidence of local recurrence at the time of data analysis.

Discussion/Conclusion: SRS for treatment of nasal lymphoma allows shorter treatment time and increased sparing of normal tissues by avoidance of normal tissues rather than fractionation of total dose. All patients tolerated SRS and acute side effects were minimal. Late side effects included chronic rhinitis and alopecia. Patient follow-up will continue until median survival is met. Limitations of this study include small sample size, and lack of follow-up CT and histopathology to confirm complete remission.
Dosimetry of Continuous Motion in Strontium-90 Plesiotherapy.
J.R. Schutte, J.C. Lattimer, K. A. Selting, C. A. Maitz. University of Missouri Veterinary Medical Teaching Hospital, Missouri, 65211.

Purpose: In plesiotherapy, using a flat surfaced strontium probe, traditional dosimetry uses static fields, with 20% overlap in multi-field planning. It accepts wide dose variations, and presumes consistent overlap and spatial orientation. The literature is sparse on descriptions of applied flat applicator multi-field dosimetry.

Methods: We compared a traditional static, multi-field application technique to that of a continuous motion dose application for 3 sample treatment fields (circular, curve-linear and clover-leaf). Four operators administered treatments a total of three times each to Gafchromic RTQA2 film under 2 mm of bolus. Dose target was 5 Gy at surface.

Results: Data were analyzed measuring the following: dose homogeneity, percent field coverage as compared with an idealized model of overlapping static fields, dose fall-off gradient, average-percent of target dose, and percent deviation of total field size. Continuous motion had increased homogeneity of dose to the target area, with larger percent-field coverage. Static-field dose fall-off was a smaller percent of treated field. Continuous motion had insufficient buildup in narrow field regions to reach target dose. Dose escalation of 35%-55%, dependent on field shape, was calculated for minimum 80% prescribed at 2mm.

Conclusion: Continuous motion has less variability in dose delivered but will require a dose escalation. This may be warranted as even template-guided static-field dosimetry consistently left central target regions with insufficient dosage. Because there is a broader dose fall-off at the periphery, field expansion may also be warranted. Regardless whether continuous motion is adopted, our data indicates that clinical strontium dosimetry be re-evaluated.
OUTCOME OF 9 DOGS TREATED WITH STEREOTACTIC RADIATION THERAPY FOR VERTEBRAL OSTEOSARCOMA
Swift, K, Custis, J, LaRue S. Flint Animal Cancer Center, Department of Environmental and Radiological Health Sciences, Colorado State University, Fort Collins CO 80534

Introduction/Purpose: Vertebral osteosarcoma (OSA) in the dog can be primary or metastatic. Previously reported treatments have included surgery, radiotherapy, chemotherapy, or a combination of those therapies. Regardless of treatment, vertebral OSA in the dog has carried an overall guarded prognosis. The purpose of this retrospective study is to determine patterns of failure, duration of local control and survival time in dogs with vertebral OSA treated with stereotactic radiation therapy (SRT).

Methods: The radiation oncology patient database at Colorado State University was searched for dogs with vertebral OSA treated with SRT. Information on patient demographics, oncological history, neurological examination findings, imaging reports and images, and date of death or current status was extracted. The diagnosis of OSA was based on histopathology in 7 dogs and cytology in 2 dogs, one of which was ALP positive. Survival times were calculated using Kaplan-Meier analysis and log rank tests.

Results: A total of 9 dogs were treated with SRT for vertebral OSA between 2010 and 2015. SRT protocols ranged from 1 to 5 fractions with a total prescribed dose ranging from 13.5 to 36 Gy. Six dogs had primary lesions and 3 had metastatic lesions. Neurologic score improved in 4 patients, remained the same in 4 and worsened in one. Five of the six dogs that presented with assessable spinal pain had reported improvement in pain. Overall median survival time was 135 days and median duration to local progression was 77 days. Two dogs were euthanized because of metastatic disease and 6 dogs were euthanized because of local disease progression. One dog was euthanized because of generalized, non-localizable pain. There was not a statistically significant survival difference between dogs presenting with primary or metastatic disease, or dogs that had improvement in neuro score following radiation therapy.

Discussion/Conclusion: This data suggests this protocol is effective as a palliative treatment and shows similar survival times to previously reported treatments. The data also continues to display the difficulty in controlling this tumor type. While the dose limiting structure is the late responding spinal cord, many of these patients died prior to the expected time to development of late radiation side effects. Dose escalation, either until tumor control is achieved or late radiation side effects are seen, may be warranted.
EARLY EXPERIENCES WITH SINGLE FRACTION STEREOTACTIC RADIATION THERAPY FOR INTRACRANIAL TUMORS IN DOGS

K.L. Kelsey¹, T.L. Gieger¹,², M.W. Nolan¹,² 1- Dept. of Clinical Sciences, College of Veterinary Medicine, North Carolina State University NC, 27607. 2- Center for Comparative Medicine and Translational Research, North Carolina State University, NC, 27607.

Introduction/Purpose: To describe initial experiences with a single fraction stereotactic radiation therapy (SRT) protocol, used as treatment for intracranial tumors in dogs.

Methods: A retrospective analysis of cases treated from August 2013 to April 2015 at NC State Veterinary Hospital was performed. Dogs were included if they were treated with a single fraction of SRT delivered to an intracranial tumor, regardless of tumor type. The gross tumor volume (GTV) was contoured using pre- and post-contrast, registered MRI and CT data sets. Sixteen Gray (Gy) was prescribed to 99% of the GTV with a planned simultaneous boost to the center of the GTV. No clinical target volume (CTV) or planning target volume (PTV) expansions were employed. Cone beam CT, indexed bite-block system, and a treatment couch with 6 degrees of freedom, were used for setup and delivery. Cases were reviewed and information related to patient demographics, tumor characteristics, clinical signs, and radiation plan dosimetry was collected. Dogs with brain tumors that underwent general anesthesia without SRT served as a control population to determine whether this SRT protocol increased risk of dying within the first 48 hours of treatment. Risk was compared using a Fisher’s exact test.

Results: Twenty nine cases were included. Median survival time cannot be determined, as 22/29 dogs were alive at the time of data analysis. The median follow-up time was 169 days in all subjects, and 250 days in those alive at the time of data analysis. Four dogs experienced acute worsening of neurologic signs in the first 48 hours after SRT. Two of these dogs did not recover from anesthesia and the other two dogs were medically managed in the hospital and recovered. There was no identifiable difference in risk of dying within 48 hours of anesthesia in dogs with brain tumors that received SRT versus not.

Discussion/Conclusions: Single fraction SRT has been used to treat intracranial tumors in 29 dogs with limited adverse events. Continued accrual and follow-up will be necessary to confirm low toxicity and characterize clinical efficacy.
GLYCOLYTIC PHENOTYPING OF CANINE MAST CELL TUMORS
L.R. Griffin, D. Thamm, E. Ehrhart, A. Marolf, E. Randall

PURPOSE: To attempt to correlate standard uptake value maximum (SUV\text{max}), as obtained by F-18 FDG PET-CT, to the grade and metastatic potential of canine mast cell tumors (MCT). This is a pilot study with the primary focus of objectively establishing that more aggressive MCT’s have an increased reliance on glucose to support their phenotype. This increased reliance on glucose is due to the Warberg effect, where neoplastic cells switch from utilizing oxidative phosphorylation to aerobic glycolysis. The underlying mechanisms and mutations that allow for this switch are currently unknown. If a definitive link between the grade of MCT and the SUV\text{max} of these tumors can be proven, it would establish canine MCTs as an acceptable translational model for further investigation of this phenomena. If the hypothesis that higher grade, metastatic MCT’s have a higher SUV\text{max} holds true, genetic profiling of canine MCT’s may allow for the identification of a mutation that supports this phenotype.

METHODS: Patients were admitted into this study if there was a cytologic or histologic confirmation of a cutaneous or subcutaneous MCT. Study funds covered the cost of traditional staging (thoracic radiographs, abdominal ultrasound) as well as a full body F-18 FDG PET-CT. After allowing for decay of the F-18 FDG, the primary tumor, any newly identified masses, locoregional lymph nodes and the spleen were sampled. Biopsies of the primary tumor were submitted for grading and a validated MCT profile. Grades of mast cell tumors were categorized as high grade or low grade and SUV\text{max} of the tumors were determined and compared to evaluate for statistical significance. Other markers of proliferation and aggressiveness (such as Ki-67, cKit mutation status and cKit distribution) were also examined.

RESULTS: A total of 10 dogs were admitted to this study. Due to the small numbers admitted, there was no statistical significance of MCT grade or proliferation markers to SUV\text{max}. A trend towards higher grade tumors having a higher SUV\text{max} was established. Splenic SUV\text{max} did not correlate with presence of splenic mastocytosis. F-18 FDG PET-CT allowed for identification of multiple other regions of concern over traditional staging methods (ie. allowed for upstaging).

CONCLUSIONS: In conclusion, SUV\text{max} measurements, as obtained by F-18 FDG PET CT, in canines affected with cutaneous or subcutaneous MCT, shows a trend towards levels being reflective of grade and aggressiveness of the primary tumor. As a follow up to this initial pilot project, funds are being acquired to allow for genetic profiling of the biopsies already obtained from these patients. In doing so, it is hoped that a genetic mutation can be determined that allows for an increased utilization of glucose by more aggressive MCTs. This would, in turn, establish a novel therapeutic target that could be investigated.
EXPRESSION OF COX-2 AND NAG-1 IN CANINE INTRANASAL CARCINOMA

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Introduction: Nasal tumors comprise approximately 2\% of all canine tumors. The current standard of care is radiation therapy (RT) and surgery. In the majority of cases, the prognosis is guarded to poor. Local recurrence is the most common cause of treatment failure. New ways to slow or prevent recurrence without significant side effects and additional prognostic factors need to be identified. Nonsteroidal anti-inflammatory drug activated gene-1 (NAG-1) and cyclooxygenase-2 (COX-2) are suspected to have a reciprocal relationship in a variety of tumors in humans, which lead us to hypothesize that this relationship exists between COX-2 and NAG-1 in canine intranasal carcinomas, and that immunohistochemical (IHC) signal intensity and distribution correlate with well-known prognostic factors and previous use of nonsteroidal anti-inflammatory drugs. One of the methods of induction of NAG-1 is through blockade of COX-2. Activation of NAG-1 has been shown to lead to cell apoptosis in vitro.

Methods: Purdue University Veterinary Teaching Hospital medical records between 2003-2014 were reviewed, identifying dogs with histologically confirmed intranasal carcinoma. Patient demographics, clinical presentation, staging test results, histopathological data, treatment, and outcome were collected. Rhinitis and normal nasal mucosa cases were included as controls. All samples were stained for COX-2 and NAG-1. Statistical analysis was performed using commercially available software.

Results: Eighty-two dogs with intranasal carcinoma were included in the study. Fifty-two patients were male and 30 were female, with median age of 10.4 yr (range 4.9-14.4) and median weight of 25.6 kg (range 4.6-58.5). Seventy six percent were presented with epistaxis and 27\% had facial deformity. Of 24 dogs that were assessed for local lymph node involvement 8\% were positive. Based on computed tomography studies and using the Modified Adams Staging System, 48\% had stage 4, 42\% stage 3, 8\% stage 2 and 3\% stage 1. Nonsteroidal anti-inflammatory drugs were given to 28\% of dogs within one month before biopsy. Twenty nine percent were treated with palliative or definitive RT. Analysis of IHC signal intensity and distribution of COX-2 and NAG-1 is currently ongoing.

Conclusion: Immunohistochemistry for NAG-1 and its relationship with COX-2 have not been described in veterinary medicine. The data obtained in this study may identify new prognostic factors and new targets for therapy.