Journal of Veterinary Internal Medicine
Open Access

J Vet Intern Med 2017;31:1572–1604

2017 ACVIM Forum Research Report Program

2017 ACVIM Forum Research Report Program
National Harbor, Maryland, June 8–9, 2017
Index of Abstracts

THURSDAY, JUNE 8

Time	Presenting Author	Abstract Title
CARDIOLOGY		
2:10 PM	Leona Wall	Development of a Standardized, Individual, Submaximal Treadmill Exercise Test in Healthy and CHIEF B1/B2 Dogs
2:35 PM	Rikke Buhl	Implantable Cardiac Loop Recorders – a Novel Diagnostic Tool for Atrial Fibrillation Detection in Horses
3:10 PM	David Connolly	Epigallocatechin-3-gallate Recouples Myofilament Calcium Sensitivity to Troponin I Phosphorylation in Feline Hypertrophic Cardiomyopathy
3:35 PM	Susanne Stieger-Vanegas	Early Experiences with 3D Modeling and Printing of Hearts with Complex Cardiac Disease
4:25 PM	Marisa Ames	Use of Moxidectin/Imidacloprid and Doxycycline For Non-Arsenical Heartworm Adulticidal Therapy
4:50 PM	Lisa Freeman	Validation of a Quality of Life Survey for Owners of Dogs with Heart Disease
5:25 PM	Melanie Hezzell	Influence of Chronic Kidney Disease on Measurements of Cardiac Structure and Function in Dogs
5:50 PM	Lauren Markovic	Accuracy of Angiographic Measurements During Transcatheter Procedures: Comparison of Two Calibration Methods in 25 Dogs
NEUROLOGY		
2:10 PM	Sofia Cerda-Gonzalez	Use of 3T Magnetic Resonance Imaging to Analyze Craniocervical Junction Cerebrospinal Fluid Flow in Cats
2:35 PM	Filippo Adamo	Biomechanical properties of Virgin PEEK, Glass-Fiber PEEK, and Carbon-Fiber-Reinforced PEEK in the Adamo Spinal Disc™
3:10 PM	Heidi Barnes Heller	Evaluation of Risk Factors in the Development of Inflammatory Brain Disease in Dogs
3:35 PM	Heidi Barnes Heller	Serum Levetiracetam Concentrations After Chronic Administration of Once Daily Extended-Release Levetiracetam in Healthy Cats
4:25 PM	Allison Bradbury	Experimental Therapies for Canine Krabbe Disease
4:50 PM	Heather Gray-Edwards	Gene Therapy in Animal Models of the Gangliosidoses: From Presentation to Human Clinical Trials
5:25 PM	Brittney Gurda	AAV Gene Therapy Studies in the Feline Model of Niemann-Pick Type C

Table 1. SDMA level, creatinine level, and SDMA-to-creatinine ratio (SDMA:Creatinine) for 52 dogs with lymphoma. Results are grouped by status of lymphoma burden and immunophenotype determined by flow cytometry. Groups are not mutually exclusive. (RI: reference interval).

Status	N	SDMA mean, median (range) [% >RI 0–14 μg/dL]	Creatinine mean, median (range) [% > RI 44–133 μmol/L]	SDMA:Creatinine mean, median (range)
Untreated	36	18, 16 (5–90) [72%]	97, 81 (47–313) [12%]	0.21, 0.19 (0.06–0.53)
CR	19	10, 11 (4–18) [11%]	90, 79 (24–169) [17%]	0.12, 0.11 (0.06–0.24)
PR	6	16, 16 (14–19) [83%]	90, 78 (65–152) [17%]	0.22, 0.20 (0.14–0.35)
Relapse	5	27, 21 (14–39) [80%]	129, 105 (71–216) [40%]	0.21, 0.20 (0.15–0.27)
B-cell	13	20, 15 (5–90)		
T-cell	6	18, 19 (10–24)		

dogs achieve CR, and that SDMA should not be interpreted in these dogs as evidence of age-related chronic kidney disease. SDMA might have potential as a biomarker of treatment response in some dogs, although the data are insufficient to make firm conclusions in this regard. The data may be underpowered to detect relationships of SDMA to immunophenotype or other characteristics of the patients or malignancy. The pathophysiology of increased SDMA in dogs with lymphoma is unknown. If the assumption is correct that SDMA production is not increased by lymphoma, potential mechanisms include 1) reversible acute kidney injury, and 2) reversible decrease in SDMA excretion without compromise to other aspects of kidney function, with either of these mechanisms being secondary to renal infiltration below the threshold of routine sonographic detection, or kidney injury resulting from spontaneous tumor lysis.

SERUM INFLAMMATORY CYTOKINE VALUES IN CACHECTIC AND NON-CACHECTIC CATS WITH CANCER AND NORMAL CATS. Erika L. Krick, Kathy Michel, Molly Church. University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA, USA

Cancer cachexia is a complex syndrome in humans associated with poor tolerance and response to treatment. Patients often have elevated serum inflammatory cytokines. Some cancer-bearing cats exhibit clinical signs of cancer cachexia. The study purpose was to compare body weight, body condition, complete blood count, serum chemistry and inflammatory cytokine values in cachectic and non-cachectic cancer-bearing cats and healthy cats.

Client-owned cancer-bearing and healthy cats prospectively underwent weight measurement, body condition and muscle mass scoring, complete blood count and chemistry panel, and serum amyloid A and alpha1-acid glycoprotein measurement. Cachexia was defined as muscle mass score below 2 and/or body condition score below 4.

Seventy-two (17 cachectic, 27 non-cachectic, 30 healthy) cats have been enrolled. Mean body weight and body condition score were not significantly different among groups. Cachectic cats had significantly lower hematocrit and albumin compared to non-cachectic ($P < 0.0001$, $P < 0.0001$) and healthy cats ($P < 0.0001$, $P = 0.0003$). Cancer-bearing cats had significantly higher white blood cell counts compared to healthy cats ($P < 0.0001$). Preliminary cytokine results showed that cachectic cancer-bearing cats had significantly higher serum amyloid A compared to non-cachectic and healthy cats ($P = 0.0086$, $P = 0.05$).

The similar body condition score and weight among all groups underscores the importance of specifically assessing muscle mass in cats with cancer. Differences in hematocrit, albumin, and serum amyloid A in cachectic versus non-cachectic cats suggest that therapies directed to the altered metabolic state of these cats combined with cytotoxic treatment is worth investigation.

EFFICACY AND SAFETY OF ELECTROCHEMOTHERAPY IN THE TREATMENT OF SOFT TISSUE SARCOMAS IN DOGS. Ron Lowe[1], Filippo Torrigiani[2], Alessio Pierini[3], Joe Impellizeri[4], George Lubas[5]. [1]Aisleigh Veterinary Clinic, Knaresborough, England, United Kingdom, [2]Dept. Veterinary Sciences, University of Pisa, San Piero a Grado, Pisa, Toscana, Italy, [3]Dept. of Veterinary Sciences, University of Pisa, San Piero a Grado, Pisa, Toscana, Italy, [4]Veterinary Oncology Services, PLLC Visiting Scholar-Vassar College, NY Director, Barrymore Center for Advanced Cancer Therapeutics, New York, NY, USA, [5]University of Pisa, Dept. Veterinary Sciences, San Piero A Grado, Pisa, Toscana, Italy

Soft Tissue Sarcomas (STS) represent up to 15% of all skin and subcutaneous tumours in dogs. Local tumour control with wide surgical margins or a combination of surgery and radiation therapy is the standard of care in the management of STS, however these approaches are not always possible due to anatomic location and/or expense of the treatment. Electrochemotherapy (ECT) is an emerging, locally ablative technique now available in the United States. ECT has been available in Europe for over a decade and is a standard therapy for cancer treatment in people and animals.

The purpose of this study was to evaluate the safety and efficacy of ECT with intravenous bleomycin in the treatment of STS in dogs.

Fifty-three client owned dogs with 55 STS were enrolled (two dogs each had two STS in different anatomical sites). Four dogs with STS located orally were excluded according to Bray (2016). Tumour location, size, histologic grade, electroporation parameters, recurrence rate, recurrence time, disease free interval (DFI) and treatment toxicity were evaluated. The owners elected to pursue ECT as an alternative treatment to surgery and/or radiotherapy. For all dogs, the diagnosis of STS was based on histopathology. Most dogs were staged with physical examination, fine needle aspiration of regional lymph node (if palpable) and three view thoracic radiographs. Complete blood cell count, minimal serum biochemistry profile and urinalysis were also obtained pre general anesthesia. For ECT treatment, dogs were premedicated with medetomidine (0.01 mg/kg, IM) and butorphanol (1 mg/kg, IM). Once sedated, patients were pre-oxygenated via face mask, and anesthesia was induced with intravenous alfaxalone (2 mg/kg). Dogs were intubated and anesthesia was maintained with oxygen, nitrous oxide and isofluorane. Atipamezole (0.05 mg/kg IM) was administered to reverse medetomidine at the conclusion of the procedure. Bleomycin was diluted in saline solution and administered IV at a dosage of 15,000 UI (Pharmacopeia Europe)/m^2 (equivalent to 15 U-US Pharmacopeia /m^2). Treatment areas were prepared for surgery, skin was clipped and aseptically prepared with povidone-iodine wash (10% iodine) and surgical spirit. All dogs received anti-inflammatory and pain medicine in the peri-operatory period with meloxicam (0.2 mg/kg SC) and butorphanol. After ECT, all patients received antibiotic coverage (Amoxicillin + Clavulanic acid 12.5 mg/kg, BID, PO or Clindamycin 5.5 mg/kg BID PO) for at least one week. Patients were assessed every 3–10 days for the initial 4 weeks after ECT treatment, then monthly for three months. Thereafter, progress was monitored until at least 2 years either by examination of the patient or by telephone contact with the owner. Any progression in the treated tissue was recorded by digital camera images. ECT was performed using Cytopulse PA4000 in 9 cases or Cytopulse Oncovet in 46 cases (Cyto Pulse Sciences, Inc., now distributed by

BTX Harvard Apparatus, MA, USA), with Gehl needle electrodes of 1–2.5 cm length from the same manufacturer. The pulse pattern employed was 8 monophasic square pulses of 100 microseconds each at a frequency of 1 Hz with the PA4000, or 1 Hz or 5 kHz with the Oncovet. The electrode pattern comprised two parallel rows of six 1–2.5 cm length needles with rows 6 mm apart. The pulse amplitude was 600–720 volts (1000–1200 volts/cm). The time between bleomycin injection and pulse delivery was 8 minutes, and maximum electroporation treatment time was 20 minutes (Tozon et al. 2016). Patients were divided into three categories according to the ECT modality. (1) ECT alone, performed in smaller lesions, where STSs were clearly visible macroscopically and could be resected by conventional surgery but the owners elected to pursue ECT. (2) intraoperative ECT, performed in larger lesions. In these cases ECT was performed at the same time of the surgical cytoreduction of the tumour. During surgery the majority of the tumour was excised, with no attempt on obtaining complete margins (as standardly accepted of 2–3 cm according to Bray 2016), and ECT was applied to lateral and deep margins before wound closure; in some cases macroscopic tumour was still present. This method was used where radical excision would have resulted in functional or cosmetic compromise due to anatomic limitation. (3) post-operative (adjuvant) ECT; this method was applied when the surgical resection of the tumour was initially performed attempting wide margins but where histological examination showed inadequate margins. Adjuvant ECT was applied after a period of 2–4 weeks from the surgical intervention (mean time 22.4 days). The reason for the delay was to perform ECT treatment as early as possible after adequate wound strength had developed following surgery and the final decision was left to the surgeon's judgement. In dogs receiving ECT alone, the tumour plus a 1–2 cm margin in all planes into grossly normal tissue were accessed by penetration of the electrode needles. The treatment was started in the margins and progressed concentrically into the tumour mass, thus avoiding transference of tumour cells from the centre to the margins. Moreover, this pattern of pulse application is reported to achieve better reduction of the blood flow to the tumour thus obtaining a better drug retention into the tumour stroma (Cemazar et al. 2016). Similarly, when ECT was used intra-operatively, a 1–2 cm margin in all directions was used. In dogs treated with ECT adjuvant to surgery, where there was no macroscopic disease, the treatment margin extended at least 1.5 cm from the healed surgical scar site in all planes. Local tumour response in dogs treated with ECT alone was evaluated according to the response evaluation criteria for solid tumors established by the veterinary cooperative oncology group consensus document (Nguyen et al. 2015). A complete remission (CR) was defined as total reduction of the tumour. A partial remission (PR) was defined as $\geq$ 30% reduction in tumour diameter. Stable disease (SD) was defined as < 30% reduction in tumour diameter or < 20% increase in tumour diameter, and progressive disease (PD) was defined as $\geq$ 20% increase in tumour diameter. The presence of new lesions near to the primary tumour was considered as PD. A minimum duration of two to three weeks was required for a response to qualify as positive. In order to assess the local treatment toxicity a grading score (5-point scale) for tissue necrosis was established by the authors and previously described (Lowe et al, 2016): 0 = none, 1 = slight swelling, 2 = swelling/necrosis < 1 cm, 3 = severe swelling, 4 = deep necrosis and 5 = severe swelling and tissue loss. DFI was calculated from the date of treatment with ECT to the first recurrence or death of the animal unrelated to the tumour; or alternatively when we censored the DFI at the date we prepared this paper. The statistical analysis was performed using Chi-squared test and Fisher's exact test.

Of the 53 dogs included in the study, 22 were females (16 neutered) and 31 were males (14 neutered). The majority of dogs were pure breeds (38/53, 71.6%); Labrador Retrievers (8) and Staffordshire Bull Terrier (5) were over represented. Patient age ranged from 4 to 15 years (median 9.1). Tumour grade was assessed in 46 cases, most tumours were grade I (21/46, 45.6%) and II (23/46, 50.0%), only two were grade III (4.4%). The large majority of tumours affected the limbs (42/55, 76.4%), other locations were: trunk (8/55, 14.5%) and head (5/55, 9.1%). Tumour size ranged from 0.4 to 20 cm (median 4.5 cm). Median follow-up period was 482 days (range 8–2,483). The first ECT treatment was performed as follows: ECT alone in 5 cases, intraoperative ECT in 26 and postoperative (adjuvant) ECT in 24 cases. Five dogs underwent a second treatment due to tumour recurrence, in 3 of them a further recurrence occurred and a third ECT treatment was performed. The treatment response in the ECT alone group was as follows: two CR, one PR and two SD. At the end of the observation period, twenty-two dogs had died, of these, 7 had tumour recurrence, which was the reason for euthanasia in two cases. Of the other 29 dogs, 8 had tumour recurrence and in three cases the affected limb was amputated as rescue treatment. Patient outcome was not available in four cases. Overall, tumour recurrence rate (OTRR) was 27.2% (15/55). Recurrence rate was not associated with tumour grade, anatomical site, tumour size, pulse frequency and pulse voltage ($P > 0.05$). For all dogs, median DFI was not reached. For dogs with tumour recurrence, median DFI was 68 days (range 0–1,025). None of our patients developed systemic adverse effects related to the ECT treatment. Local toxicity was well tolerated in 65% of cases (36/55 had toxicity score $\leq$2 in a scale with 5 as maximum) and was not associated with tumour grade, tumour size and pulse frequency ($P > 0.05$). Local toxicity was associated with higher pulse voltage (1000 vs. 1200 V), which was statistically significant ($P = 0.003$).

The overall tumour recurrence rate (OTRR) of ECT alone or in combination with surgery (intra or post-operative) was 27.2%

Adjuvant ECT with local injection of bleomycin has been successfully applied in the treatment of canine sarcomas in a previous study (Spugnini et al. 2007). However, these results cannot be compared with ours because the tumour list included neoplastic entities that are no more considered as "true canine STS" (i.e. hemangiosarcoma, malignant fibrous histiocytoma, leiomiosarcoma and neurofibrosarcoma) (Liptak & Forrest 2013). Moreover the criteria of tumour response (i.e. complete response and progressive disease) were not extensively illustrated in the paper thus making a comparison impossible.

Other therapies including adjuvant radiation therapy and intralesional chemotherapy have been reported to have an OTRR of 18.0% and 16.6%, respectively (Demetriou et al. 2012, Havlicek et al. 2009). When possible, a wide margin excision still remains the best choice to treat canine STS (3.2%, Prpich et al. 2013). In this study, ECT with intravenous bleomycin was well tolerated with 65% showing mild toxicity. This finding is similar to the results previously reported by one of the authors using the same toxicity score scale (53%, Lowe et al. 2016). To our knowledge, no data has been reported regarding postsurgical time of healing or complication rate with intraoperative ECT. Local toxicity was similar in intraoperative and postoperative ECT groups, suggesting that treatment delay may be not necessary in a postoperative setting.

ECT with bleomycin should be considered an option to treat STS in dogs especially when other treatment options are declined or not applicable. However, further investigation is necessary to identify ideal treatment parameters.

Bray JP, Soft Tissue Sarcoma in the Dog – Part 1: A Current Review, *Journal of Small Animal Practice*, 57:510–9, 2016.

Chase D et al., Outcome Following Removal of Canine Spindle Cell Tumours in First Opinion Practice: 104 Cases, *Journal of Small Animal Practice*, 50: 568–74, 2009.

Cemazar M et al., Efficacy and safety of electrochemotherapy combined with peritumoral IL-12 gene electrotransfer of canine mast cell tumours, *Veterinary and Comparative Oncology*, 2016.

Demetriou JL et al., Intentional Marginal Excision of canine Limb STSs Followed by RT", *Journal of Small Animal Practice*, 53: 174–81, 2012.

Havlicek M et al., Intra-Operative Cisplatin for the Treatment of Canine Extremity Soft Tissue Sarcomas, *Veterinary and Comparative Oncology*, 7: 122–9, 2009.

Liptak & Forrest in Withrow SJ, Page R, and Vail DM, *Withrow and MacEwen's Small Animal Clinical Oncology*. Elsevier Health Sciences, 2013.

Lowe R et al., The treatment of canine mast cell tumours with electrochemotherapy with or without surgical excision, *Veterinary and Comparative Oncology* (2016).

Nguyen SM et al., Response evaluation criteria for solid tumours in dogs (v1. 0): a Veterinary Cooperative Oncology Group (VCOG) consensus document, *Veterinary and Comparative Oncology,* 13: 176–83, 2015.

Prpich CY et al., Second Intention Healing after Wide Local Excision of Soft Tissue Sarcomas in the Distal Aspects of the Limbs in Dogs: 31 Cases (2005–2012), *Journal of the American Veterinary Medical Association*, 244: 187–94, 2014.

Spugnini EP et al., Adjuvant electrochemotherapy for the treatment of incompletely excised spontaneous canine sarcomas. *In Vivo*, 21:819–22, 2007.

Tozon N et al., Operating Procedures of the Electrochemotherapy for Treatment of Tumor in Dogs and Cats, *Journal of Visualized Experiments* 116, 2016.

EVALUATION OF CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY IN DOGS WITH B CELL LYMPHOMA. Nicola Mason, Kazim Panjwani, Martha MaloneyHuss. University of Pennsylvania, Philadelphia, PA, USA

Chimeric Antigen Receptors (CARs) are synthetic receptors that combine an antigen-specific antibody moiety with T cell intracellular signaling domains. T cells that have been engineered to express a CAR can therefore recognize a specific antigen in an MHC independent manner and subsequently mediate potent cytotoxic responses against cells that express the target antigen. In this study, we aimed to determine whether canine T cells could be genetically modified using a second generation, CD20 targeting CAR and whether these re-directed T cells could proliferate in response to CD20 + target cells and become CD20-specific serial killers. We used a third-generation self-inactivating lentiviral vector to successfully deliver a second generation CD20-CD28-CD3-zeta CAR to canine T cells isolated from healthy dogs and dogs with B cell lymphoma. Cells were first activated using artificial Antigen Presenting Cells (aAPC) and then transduced with the lentiviral CAR. We demonstrate that canine T cells can be successfully re-directed and upon engagement with CD20, can undergo antigen-specific proliferation, cytokine production and serial killing. Having demonstrated proof-of-concept in vitro, we treated 4 dogs with B cell lymphoma with autologous, second generation, CD20 targeted CAR T cells. Although numbers of adoptively transferred CAR T cells were limiting, and B cell aplasia was not induced in any dog, we did observe evidence of in vivo CAR T cell activity. Taken together, this early data provides proof-of-concept that autologous CD20-targeting CAR T cell products can be generated from canine B cell lymphoma patients and should be further explored for the treatment of CD20 + malignancies.

SURVIVIN INHIBITION WITH EZN-3042 FOR CANINE LYMPHOMA THERAPY: PHASE-I INVESTIGATION. Douglas H. Thamm[1], Jenette Joseph[2], Travis Meuten[3], Kristen Weishaar[3]. [1]Colorado State University Flint Animal Cancer Center, Fort Collins, CO, USA, [2]University of Colorado Comprehensive Cancer Center, Aurora, CO, USA, [3]Colorado State University, Fort Collins, CO, USA

Lymphoma is one of the most common cancers in dogs. While remission is experienced in most dogs receiving chemotherapy, very few are cured, with median survival times typically in the 12-month range. Novel treatment approaches are needed. The IAP family member survivin, one of the most commonly overexpressed proteins in human cancer, plays a critical role in apoptosis resistance, a major cause of drug-resistant treatment failure. Therapies targeting survivin have shown promise preclinically; however, none have been evaluated in dogs to date. We demonstrated previously that survivin is abundantly expressed in canine lymphoma and osteosarcoma (OSA), and that high expression correlates with inferior clinical outcome. Furthermore, survivin inhibition with siRNA or the locked nucleic acid antisense oligonucleotide EZN-3042 reduced proliferation, increased apoptosis and enhanced chemosensitivity in canine lymphoma and OSA cells in vitro, and increased chemosensitivity in a canine OSA xenograft. The goal of this study was to investigate the safety and biologic effect of systemic EZN-3042 delivery in dogs with lymphoma. The primary endpoint was modulation of survivin expression in lymphoma tissues.

This was a prospective, phase-I dose-escalation trial in dogs with biopsy accessible multicentric lymphoma. Dogs received 3 biweekly doses of EZN-3042 as a 2-hour IV infusion. Starting dosage was 3.25 mg/kg. Escalation occurred at 1.25 mg/kg increments, according to a standard 3 + 3 cohort design. A CBC, serum biochemistry profile, coagulation profile and urinalysis were performed before the first and at each subsequent treatment. Peripheral blood mononuclear cells (PBMC) and tumor tissue were collected prior to the first treatment and 24 hours after the 3rd treatment. Adverse events (AEs) were graded according to the VCOG-CTCAE v1.1. Survivin expression was assessed in pre- and post-treatment tumor tissue and PBMCs utilizing qRT-PCR and immunohistochemistry (IHC). Tumor cell proliferation and apoptosis were assessed using Ki67 and activated caspase-3 IHC.

18 dogs were enrolled in 5 dose cohorts, ranging from 3.25 to 8.25 mg/kg twice weekly. 1 of 6 dogs treated at the highest dose cohort developed grade 3 thrombocytopenia. No other AEs were noted. Reduction in survivin mRNA was observed in PBMC and tumor tissue in 3 of 5 evaluable dogs treated at the highest dose cohort (8.25 mg/kg). Reduction in tumor survivin protein was observed in 3 of 6 cases at 8.25 mg/kg, but there was no correlation between protein and mRNA reduction. Reduction in Ki67 was observed in 2/5 cases, and increase in activated caspase was observed in 1/5 cases at 8.25 mg/kg. There was no correlation between survivin inhibition and changes in proliferation or apoptosis.

In conclusion, we have demonstrated reduction in survivin expression in lymphoma tissues and PBMC in the majority of dogs treated with EZN-3042 at a dose of 8.25 mg/kg twice weekly, a dose and schedule associated with acceptable toxicity. This biologically effective dose can be utilized in future studies evaluating EZN-3042/chemotherapy combinations in dogs with lymphoma and/or OSA.

SMALL ANIMAL INTERNAL MEDICINE

EVALUATION OF SERUM THYROXINE, FREE THYROXINE, AND THYROTROPIN CONCENTRATIONS FOR DIAGNOSIS OF FELINE IATROGENIC HYPOTHYROIDISM. Mark E. Peterson[1], Rhett Nichols[2], Mark Rishniw[3]. [1]Animal Endocrine Clinic, New York, NY, USA, [2]Antech Diagnostics, Lake Success, NY, USA, [3]Cornell University, Ithaca, NY, USA

Radioiodine is generally considered the treatment of choice for feline hyperthyroidism but can cause iatrogenic hypothyroidism in up to 75% of cats. However, these hypothyroid cats rarely develop overt clinical signs of the disease (hair-coat changes), and there are no published guidelines for how to diagnose or manage iatrogenic hypothyroidism in cats. Treating hyperthyroidism can also unmask subclinical chronic kidney disease (CKD), with up to 49% of cats developing azotemia by 3–6 months of treatment. Cats with iatrogenic hypothyroidism are more likely to develop CKD than treated cats that remain euthyroid; iatrogenic hypothyroidism can also reduce survival time, especially in cats with concurrent azotemia.Therefore, it is important to diagnose hypothyroidism in these cats, since thyroid hormone replacement might preserve kidney function and improve survival.

In this study, we sought to determine which serum thyroid hormone or thyrotropin test best identifies iatrogenic hypothyroidism in cats that first develop azotemia after radioiodine treatment. Further, we sought to determine which test would best differentiate these azotemic, hypothyroid cats from azotemic sick euthyroid cats following radioiodine treatment, as well as from azotemic cats with CKD but no history of thyroid disease.

Five hundred and twenty-four hyperthyroid cats treated with radioiodine at the Animal Endocrine Clinic from June 2013 to June 2015 were evaluated for inclusion in this study. None of these cats had pre-existent azotemia (defined as serum creatinine >1.9 μg/dL), either when hyperthyroid or controlled with methimazole. Following radioiodine, 42 cats that developed post-treatment azotemia (creatinine >2.5 μg/dL) had serum concentrations of thyroxine (T4), free T4 by dialysis (fT4), and thyrotropin (TSH) measured at 3, 6, and 12 months. Iatrogenic hypothyroidism was confirmed ($n = 28$) or excluded ($n = 14$) in these 42 cats on the basis of thyroid scintigraphy. Fourteen cats with CKD and 166 clinically normal cats underwent similar serum thyroid testing and scintigraphy. Nineteen of the 28 cats with documented hypothyroidism had T4, fT4, and TSH reevaluated after 1–3 months of levothyroxine (L-T4) treatment to determine the influence of replacement therapy on these analytes.