

4th Bi-Annual Symposium Annapolis, Maryland ~ September 1st and 2nd 2017

VNS Business Meeting 8:00-8:30 Successful treatment of hydrocephalus, syringopontia, 8:30-9:00 А syringobulbia and syringomyelia due to a 4th ventricle Roynard arachnoid diverticulum by direct diverticulectomy in a dog Т Transsphenoidal surgery in the dog and cat (Part 1) 9:00-10:00 Owen Break 10:00-10:15 10:15-11:15 Т Transsphenoidal surgery in the dog and cat (Part 2) Martin Т 11:15-12:15 Case presentations; Transsphenoidal surgery Chen 12:15-2:00 Lunch on own Tolerability and initial efficacy of convection-enhanced delivery of combinatorial IL-13RA2 and EphA2 targeted cytotoxins to 2:00-3:00 Т Rossmeisl dogs with spontaneous intracranial malignant gliomas Novel immune checkpoint inhibitor enhances response to vaccine-based immunotherapy in dogs with high-grade glioma 3:00-3:30 А Pluhar Break 3:30-3:45 **Round table discussion** 3:45-6:00 Transsphenoidal Surgery Welcome reception 6:30

PROGRAM – Friday, September 1st

Successful treatment of hydrocephalus, syringopontia, syringobulbia and syringomyelia due to a fourth ventricle arachnoid diverticulum by direct diverticulectomy in a dog

Patrick Roynard, DVM, MRCVS; <u>proynard@livs.org</u> Long Island Veterinary Specialists, Plainview, NY, USA

A 6.5 month old female intact Great Dane presented with vestibular tetra-ataxia, tetraparesis, and cervical scoliosis associated with hydrocephalus and extensive syringohydromyelia found on previous MRI examination. CT and MRI examination at our facility showed hydrocephalus, syringopontia and syringobulbia with atrophied brain tissue, syringohydromyelia in the entire spinal cord, and cervical kyphoscoliosis due to a fourth ventricle arachnoid diverticulum. Surgical treatment was performed with complete diverticulectomy after suboccipital craniectomy, cranioplasty and placement of a ventriculoperitoneal shunt (VPS) in the left lateral ventricle. Recovery from the surgery was uneventful initially. Six days post-operatively, the patient developed a fever and relapse of cervical pain. MRI examination, cerebrospinal fluid (CSF) analysis and culture 9 days post-operatively were consistent with aseptic meningitis. The patient was treated medically and clinical signs improved. At 6 and 12 months post-operatively, neurological examination was markedly improved. MRI re-examination at 6 and 12 months revealed resolution of the hydrocephalus, syringopontia and syringobulbia, along with improvement of the syringohydromyelia. To the author's knowledge, this is the first report of successful, MRI-documented long-term outcome of direct surgical removal of an arachnoid diverticulum in the fourth ventricle in a dog. Post-surgical aseptic meningitis is a possible complication and a relapse of cervical pain after surgery may be only temporary and should not warrant euthanasia.

Transsphenoidal surgery in the dog and cat (Part 1 and 2)

Tina Owen, DVM, DACVS and Linda Martin, DVM, DACVECC; <u>tinajoowen@vetmed.wsu.edu</u>; <u>Igmartin@vetmed.wsu.edu</u> Washington State University, Pullman, WA, USA

Dogs and cats with sellar masses typically present in one or more ways: 1) with neurologic symptoms, 2) with endocrine abnormalities or 3) as an incidental finding on a computed tomography (CT) or magnetic resonance (MR) imaging performed for some other reason. Functional (endocrine excess) and non-functional pituitary tumors and other sellar and parasellar masses can be treated by transsphenoidal surgery (TS) in the dog and cat. There is an exponential learning curve with this procedure and post-operative management of these cases requires a cohesive team of specialists. Case selection, pre-operative work-up and surgical indications for dogs and cats with sellar masses will be discussed as well as immediate and long-term care and post-operative complications. The goals of this presentation are: 1) Understanding the importance of identifying sellar masses with advanced imaging. 2) Knowing when TS is an appropriate treatment option. 3) Knowing surgical risks, complications and the immediate post-operative management associated with this procedure. 4) Understanding the long-term management and follow-up required after discharge from the surgical facility.

Transsphenoidal surgery in the dog and cat (Part 3, Case presentations)

Annie Chen, DVM, DACVIM (Neurology); <u>avchen@vetmed.wsu.edu</u> Washington State University, Pullman, WA, USA

Three cases will be presented discussing the clinical presentation, treatment and longterm outcome. Case #1: Vince, 8 yr. MN Goldendoodle. Presented to the family veterinarian for lethargy and being less playful January 2015, diagnosed with Cushing's disease July 2015, started on Trilostane. Neurologic signs including dull mentation and circling to the left developed in December 2015, MR imaging at that time revealed a pituitary mass with a P/B (pituitary height/brain area) ratio 1.00*. Case #2: Otto, 14 yr. MN DSH. Presented to the family veterinarian for abdominal pain after eating and increased water consumption, January 2015. Otto was diagnosed with diabetes mellitus which progressed to uncontrolled diabetes. May 2015 Otto began to show signs of acromegaly with an increasing broad face and enlarging mandible. An MR image revealed a pituitary mass with a P/B ratio of 0.66*. Case #3: Sampson, 9 yr. MN Boxer. Presented to the family veterinarian for ataxia, anorexia (owners were hand feeding) and loss of vision over a 2-3 month period. November 2014, Sampson had MR imaging and was diagnosed with a non-functional (lack of endocrine signs, normal endogenous ACTH, 6.1 pmol/L) sellar mass with a P/B ratio of 1.30*.

*P/B ratio was calculated from MR imaging as height of the pituitary gland in mm/area of the brain in cm2 (normal)

Tolerability and initial efficacy of convection-enhanced delivery of combinatorial IL-13RA2 and EphA2 targeted cytotoxins to dogs with spontaneous intracranial malignant gliomas

John Rossmeisl, DVM, DACVIM (Neurology); <u>irossmei@vt.edu</u> Virginia Tech, Blacksburg, VA, USA

The IL-13RA2 and EphA2 receptors are attractive targets for malignant gliomas, being expressed in ~90% of canine and human gliomas, and absent in normal brain. Here, we report a Phase I trial in dogs with gliomas to determine tolerability of IL-13RA2- and EphA2- targeted recombinant Pseudomonal and Diphtheria cytotoxins administered using convection enhanced delivery (CED). Clinical signs of forebrain dysfunction and histopathologically confirmed glioma demonstrating IL- 13RA2 or EphA2 immunoreactivity were required for inclusion. A 3+3 dose-escalation design was used, with cohorts administered 0.05, 0.1, 0.2, or 0.4 µg of each cytotoxin/ml infusate. CED planning using a patient-specific shape fitting algorithm simulated optimum cannula placement and target coverage prior to treatment. CED was performed using refluxpreventing cannulae to co-administer cytotoxins with gadolinium, which allowed intraoperative MRI visualization of infusions. Dose-limiting toxicities (DLT) were defined as grades 3, 4, or 5 adverse events within 28 days of infusion. Clinical, laboratory, and brain MRI examinations were performed on days 14, 28, 42, 84, and 180 following treatment. Ten CED infusions have been performed in nine dogs with unresected gliomas. Median target volume was 5.63 cm3 (0.69 to 11.4 cm3). Median duration of infusion was 2.9 hours. Median target coverage was 78% (38-94%). MRI monitoring facilitated revisions and continued target infusion after observation of infusion complications in 3 cases. Durable clinical and objective partial tumor responses (52-95% decreases) have been observed in 5/8 dogs with >12 weeks of followup. No DLT have occurred. Tumor necrosis in infused regions was evident in 4/4 necropsies.

Novel immune checkpoint inhibitor enhances the response to vaccine-based immunotherapy in dogs with high-grade glioma

Liz Pluhar, DVM, DACVS; <u>pluha006@umn.edu</u> University of Minnesota, St. Paul, MN, USA

Glioma is the most common primary intra-axial canine brain tumor with a poor prognosis. The median survival of dogs in earlier clinical trials treated with surgery and immunotherapy was 200 days. Immune checkpoint inhibitors have been shown to enhance anti-tumor immunity for many different tumor types. We developed caninespecific peptides that inhibit the immunosuppressive effects of a novel immune checkpoint protein, CD200 (OX2). We hypothesized that the addition of these peptides to our previously tested autologous tumor lysate vaccine therapy would significantly increase overall survival (OS). Dogs were treated by standard resection and injections of autologous tumor lysate/imiguimod + anti-CD200 peptides. Vaccines were given once a week for 3 weeks, then once a month for 3 vaccines, then once every 6-8 weeks until tumor recurrence, starting 10days after surgery. MRIs were obtained immediately after and 4, 8, and 12 months after surgery. The primary outcome measured was OS. 19 dogs were recruited, primarily brachycephalic breeds with mean age of 8.1 years. All tumors were high-grade (grade III or IV) gliomas. The primary adverse effect was a steroid-responsive leukoencephalopathy; but owners assessed their dogs' quality of life as excellent. Median OS for the peptide treated dogs was 386 days, which is significantly longer that with vaccines alone from previous studies (200 days) (P=0.015). CD200 inhibitory peptides added to vaccine-based immunotherapy after tumor resection delayed tumor recurrence and significantly extended OS in dogs with spontaneous highgrade glioma.

PROGRAM – Saturday, September 2nd

8:00-8:30	А	Development an of International Canine IVDE Observational Registry: A big data approach to "little dog" problems	Moore
8:30-9:30	т	Successes and failures in surgical management of congenital spinal malformations	Carrera- Justiz
9:30-10:30	т	Advances in canine cervical vertebral column stabilization	Hettlich
10:30-10:45	Break		
10:45-11:45	т	3-D printing applications for neurosurgery	Wininger
11:45-12:45	т	Making a Confident Diagnosis of Lumbosacral Disk Disease and its Treatment	Sanders
12:45-2:15	Lunch on own		
2:15-2:45	А	Surgical Treatment of Lumbosacral Disk Disease – Technique and Results	Sanders
2:45-3:45	Т	Lumbosacral stenosis and associated complications	Bergman
3:45-4:15	А	Clinical and Preclinical Use of Pedicle Screws in Veterinary Medicine	Easley
4:15-4:30		Break	
4:30-6:00		Round table discussion Lumbosacral	
7:00-10:00		Conclusion of Symposium ~ Gala Dinner	

Development of an International Canine IVDE Observational Registry: A big data approach to "little dog" problems

Sarah Moore, DVM, DACVIM (Neurology); <u>moore.2204@osu.edu</u> The Ohio State University, Columbus, OH, USA

Client-owned (pet) dogs experience intervertebral disc extrusion (IVDE) commonly, with 20,000-30,000 new cases managed by veterinary spinal surgeons in the United States alone each year. While a large cohort of affected dogs are managed across tertiary care veterinary hospitals each year, a much smaller number are cared for at any single given facility. Thus the establishment of an observational veterinary patient registry constitutes a key step in performing epidemiologic studies and assessing the impact of therapeutic strategies to facilitate clinical research. A harmonized approach to data collection amongst veterinary clinicians can serve to facilitate multi-institutional studies. Further, accumulating information on IVDE in dogs may contribute to current "big data" approaches to enhance understanding of the disease using heterogeneous multiinstitutional, multi-species data sets from both pre-clinical and human clinical studies. Here we provide rationale and framework for this observational registry and share our experience in the establishment of what we believe is the first international veterinary patient registry of any kind. We also present preliminary data related to demographics, descriptive statistics, and future directions for advancing translational research using information accumulated via the canine observational registry.

Successes and failures in surgical management of congenital spinal malformations

Sheila Carrera-Justiz, DVM, DACVIM (Neurology); <u>carrerajustiz.s@ufl.edu</u> University of Florida, Gainesville, FL, USA

Congenital spinal malformations, specifically those seen in screw-tailed breeds, have posed a tremendous clinical challenge for many years. To date, a reliably successful treatment for those animals that develop clinical signs does not exist. This talk will present a brief review of the pathophysiology of the vertebral malformations and the theories behind the development of myelopathy in these cases. I will present a case series treated with a previously described surgical technique and discuss successes and failures.

Advances in Canine Cervical Vertebral Column Stabilization

Bianca Hettlich, Dr. med vet, DACVS; <u>bianca.hettlich@vetsuisse.unibe.ch</u> Vetsuisse Faculty, University of Bern, Switzerland

In the last decade, there has been a steep increase in the use of surgical stabilization techniques of the cervical vertebral column for dogs with cervical spondylomyelopathy (CSM). Most techniques have been reported in clinical case series, few have been compared directly in clinical or in vitro studies. This presentation will provide an overview of fixation techniques for dogs with CSM, including intervertebral spacers and rigid spinal fixation using various implants. Results of clinical studies and in vitro biomechanical studies will be presented and discussed.

3-D Printing Applications for Neurosurgery

Fred Wininger, VMD MD DACVIM (Neurology); <u>fredwininger@gmail.com</u> Veterinary Specialty Services, Creve Coeur, MO, USA

3D printing or additive manufacturing (AM) is gaining popularity for the synthesis of anatomic modeling and custom prosthetics. AM may be of particular value in veterinary medicine because of the anatomic variability in size and morphometry of patients. Aside from modelling normal anatomy, applications include craniotomy jigs and customized cranioplasty. In the spine applications include implant guidance and stabilizing/fusion apparatuses as well as potential biomechanical study devices. Images for medical AM are generally acquired from CT because of its high contrast and spatial resolution for bone though MRI can be used. Surface renderings are converted to triangular mesh networks known as manifolds that can be manipulated. The manifold is then "sliced" into layers that can be printed. Most AM printers fall into one of three categories. Because of their availability and cost, extrusion techniques such as fused deposition modeling (FDM) are the most common encountered in non-commercial use. Though useful for creating anatomic models. FDM's lower resolution and materials may limit its medical utility. Light polymerized techniques such as stereolithography solidify liquid resin into complex polymers (methacrylate). These techniques have higher resolution, are cost effective, and potentially biocompatibility. However, they have more complex post-processing and are prone to printing error. Despite their high cost, binding techniques such as selective laser sintering are attractive because of their high resolution and biocompatible/biomechanical materials such as PEEK and titanium. The scope of AM is only limited to the modeling and materials available. The customizable nature makes potential applications infinite but biomechanical validation difficult.

Making a Confident Diagnosis of Lumbosacral Disk Disease and its Treatment Sean Sanders, DVM, DACVIM (Neurology); <u>sean.sanders@mac.co</u> Seizure Sentry LLC, North Bend, WA, USA

Lumbosacral disk disease of dogs can present with a nebulous history and intermittent clinical signs that may not be specific to disease of the nervous system. Conditions resulting in similar clinical signs originating from primarily musculoskeletal and to a lesser extent, metabolic disease may appear to be classic "cauda equine syndrome". Being confident in the localization and diagnosis of the disease depends on an accurate history, physical exam, neurological exam and support from diagnostic imaging. Treatment may consist of medical management or surgery. Since many patients are working dogs and expected to continue to perform, conservative management alone is often not a viable option. Surgery, with the goal of returning the dog to work, must combine neural structural decompression, distraction and reduction of the lumbosacral junction and stabilization with a technique that not only achieves these goals but is also robust enough to withstand the rigors of a working environment. This presentation will primarily focus on attaining a confident diagnosis and the logical development of a surgical technique used to achieve the above goals.

Surgical Treatment of Lumbosacral Disk Disease – Technique and Results

Sean Sanders, DVM, DACVIM (Neurology); <u>sean.sanders@mac.co</u> Seizure Sentry LLC, North Bend, WA, USA

Lumbosacral disease is a combination of disk degeneration, instability and dynamic compression of the cauda equine affecting primarily, middle age to senior, medium to large breed dogs. Certain breeds such as the German Shepherd are known to be more commonly affected and subjected to a working environment that potentially places them at greater risk for the development of the condition. Surgical treatment should aim to achieve decompression of neural structures, as well as, distraction and stabilization of the lumbosacral junction. Being a transition zone of the spinal column, this area of the spine is subjected to potential forces that necessitate a robust implant that can withstand the activity of a working dog. Additionally, anatomic differences of the individual patient can be mitigated with an implant which can be site engineered for the patient's specific needs. This abstract will briefly discuss the development and long- term results of an implant constructed of commonly available components and used to distract and stabilize the lumbosacral junction in 93 dogs.

Complicated Cases

Robert Bergman, DVM, MS, DACVIM (Neurology); <u>rbergman@carolinavet.com</u> Carolina Veterinary Specialists, Matthews, NC, USA

Lumbosacral stenosis secondary to degenerative intervertebral disc disease generally has a successful outcome following surgical decompression of the cauda equina. However, it can be difficult to determine if a fusion/stabilization procedure may be a better choice in specific cases. Furthermore, complications can arise following routine lumbosacral decompression. This lecture will focus on decision making regarding stabilization vs. decompression. It will also discuss complications encountered with lumbosacral surgery and revision surgery with follow-up. Stabilization procedures will be discussed.

Clinical and Preclinical Use of Pedicle Screws in Veterinary Medicine

Jeremiah Easley, DVM, DACVS; <u>jeremiah.easley@colostate.edu</u> Colorado State University, Fort Collins, CO, USA

Pedicle screws, while the most common spinal implant utilized in people for nearly 30 years, have only recently been introduced into veterinary medicine. Although sparse, reports of pedicle screw use in dogs and horses exist. The surgeons in the Preclinical Surgical Research Laboratory at Colorado State University have performed over 5,000 preclinical spinal procedures in sheep utilizing pedicle screws for lateral interbody fusion and posterior spinal fusion. This experience has led to the clinical use of pedicle screws in horses for cervical fusion and dogs for lumbosacral stabilization. From our experience, pedicle screws are highly intuitive and easy to use in spinal surgery. With minimal practice, a surgeon can become comfortable with the implants and corresponding instrumentation. The use of pedicle screws in veterinary medicine is expanding and further implementation of these spinal implants will require increased/improved training to veterinary surgeons.