UC Davis Veterinary Oncology One Goal: Ending Cancer



Center for Companion Animal Health Director's Message

The oncology team at UC Davis School of Veterinary Medicine has one overriding goal: ending cancer. We work toward this goal by providing compassionate state of the art care for our animal patients and their families, education for practitioners and training for the next generation of clinicians and researchers and through a basic science and translational research program. The overview of the veterinary oncology program provides a snapshot of where we are now and where we see our program headed.



Michael S. Kent

We continue to expand our efforts in all areas of the oncology program. Specifically, we have increased our capacity within the clinic, focused on patient centered care, expanded our training programs, increased our research collaborations, and bolstered and expanded our research program.

Philanthropic support has allowed us to accomplish much of what we have done. From investing in infrastructure and equipment including helping to develop two new PET scanners, establishing a pharmacokinetics core and introducing 3D printing to patient care, developing new drugs to kill cancer and expanding our clinical trials, hiring new clinicians, research faculty and postdoctoral fellows to helping understand the genetic basis of cancer through basic science and genetic research we are working on all fronts to achieve our goal.

In the following pages, we hope to describe just some of the work we have undertaken and give you a glimpse into the future of the veterinary oncology program. We of course welcome any questions you might have and look forward to working together to end cancer.

Michael had

Michael S. Kent, DVM, MAS, DACVIM, DACVR Director, Center for Companion Animal Health Co-Director, Comparative Cancer Center Program Leader, NCI-designated Comprehensive Cancer Center

COMPASSIONATE PATIENT CARE • RESEARCH • EDUCATION

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Clinical Care is at the Heart of What We Do

Our cancer diagnostic and treatment services provide comprehensive care at one of the busiest veterinary cancer treatment centers in the world. The services we provide to dogs, cats and equine patients use both traditional and innovative approaches in treatment. The traditional approach includes chemotherapy, radiation therapy, radioactive iodine therapy and surgical intervention. Our innovative approach includes interventional radiology, immunotherapy, stereotactic radiosurgery, intensity modulated radiotherapy and computerized treatment planning.

Our clinical team consists of more than 30 faculty and staff members, including multiple full-time, board certified veterinarians in Medical and Radiation Oncology, Surgical Oncology, Radiology, and Pathology. In addition, our state-of-the-art imaging services include CT, MRI, ultrasound, nuclear medicine and PET scanning. Scientific research also contributes to our excellence in cancer treatment. Our oncology team performs basic science and clinical research that include clinical trials designed to benefit our patients by discovering new ways to treat and diagnose cancer. We collaborate extensively with fellow clinical researchers at the UC Davis Medical Center and the worldwide oncology community to develop safer and more effective treatments that lead to new advancements for both veterinary and human patients.

The patient's quality of life is our central focus.

Our oncology program is unique. Not only are we part of one of the largest veterinary teaching hospitals in the world, we are part of one of the nation's premier research universities. This combination allows us to bring the newest advances to our patients. If a pet has a complicated problem or a health crisis, we are able to provide the most comprehensive range of specialties available at one location. You can count on us to make available all the specialists of the hospital. We work very closely with other departments including Clinical Pathology, Dentistry, Dermatology, Emergency/Critical Care, Histopathology, Internal Medicine, Neurology, Ophthalmology, Radiology and Surgery. Emergency care and critical care services are available 24 hours a day, 365 days a year.

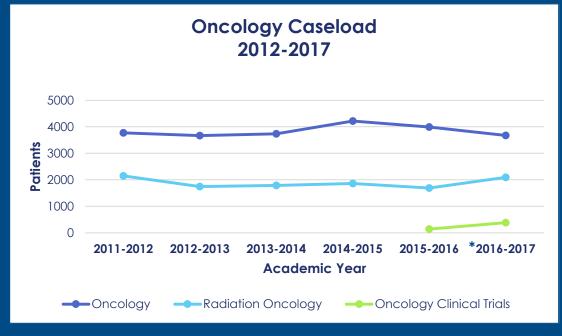
"It's clear why patients are brought here. They receive the highest standard of compassionate care and benefit from the latest discoveries in veterinary medicine."

– UC Davis Chancellor Gary S. May

Introduction to Clinical Oncology Services

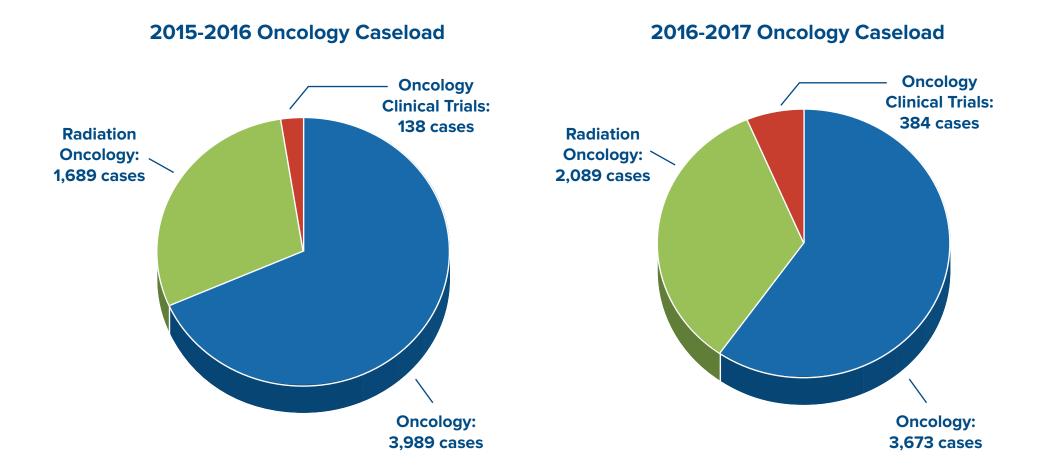
Clinical trials accelerate the identification and development of diagnostics and therapeutics for the benefit of veterinary and human patients. The UC Davis School of Veterinary Medicine's oncology patient caseload provides an excellent resource for clinical investigations due to the patient volume, variety of cases presented and the excellent research collaborations within the veterinary hospital environment.



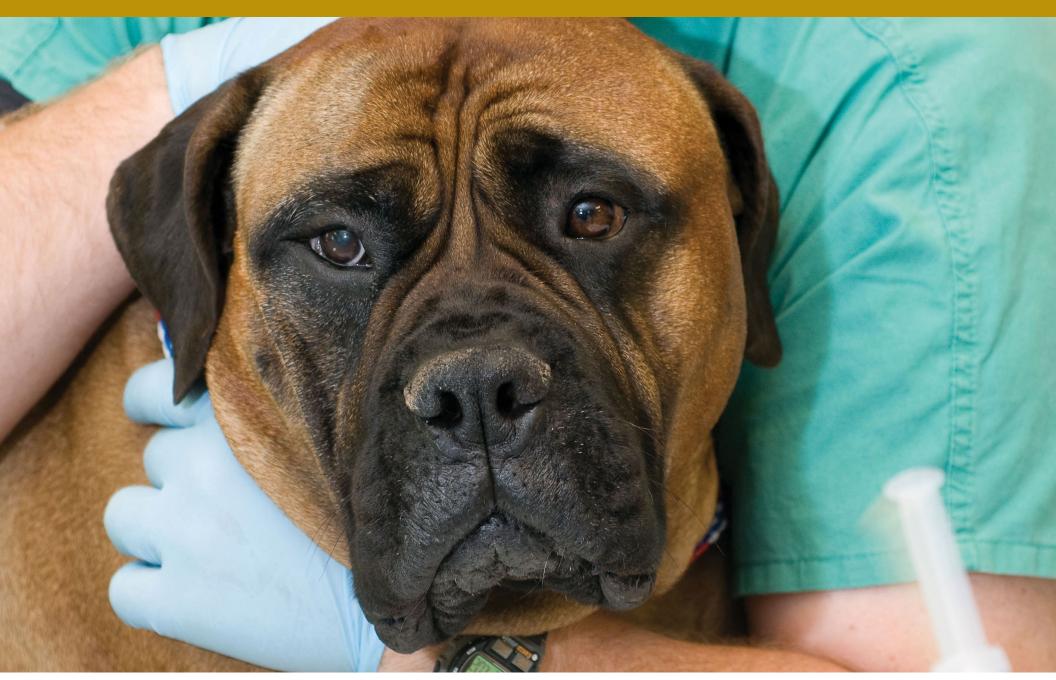


*Oncology Clinical Trial cases were not tracked separately prior to 2015.

Introduction to Clinical Oncology Services



Medical Oncology



Our Medical Oncology Faculty

Dr. Katherine Skorupski

is a native of southern California, but moved to Texas for college and received both her B.S. and DVM from Texas A&M University. She then completed two rotating internships at All-Care Animal Referral Center in Fountain Valley, California and The Ohio State University before going on to the University of Pennsylvania, where she trained as a resident in medical oncology. Following ACVIM certification in 2005, she was on staff at the University of Pennsylvania as a clinical lecturer. Dr. Skorupski joined the UC Davis faculty in 2006. She is passionate about providing excellent resident training and utilizing the clinical trials program



to better define veterinary standard-of-care as well as potential new therapeutic options for cancer patients of all species. Specific areas of research interest include histiocytic sarcoma, feline oral squamous cell carcinoma and canine osteosarcoma.

Dr. Jenna Burton

received her B.A. in Biology from Bowdoin College. She then worked as a research assistant at a biotechnology company prior to earning her DVM from The Ohio State University in 2006. She completed an internship in Small Animal Medicine and Surgery and a four-year medical oncology residency at Colorado State University. Dr. Burton is board certified in medical oncology by the American College of Veterinary Internal Medicine. Dr. Burton remained at CSU as an Assistant Professor of Oncology where she was responsible for the day-to-day management of all clinical trials at the CSU Animal Cancer Center. She joined the faculty at UC Davis in 2014 and is



currently an Assistant Professor of Clinical Medical Oncology and the Associate Director of the Veterinary Center for Clinical Trials.

Dr. Sita Withers

earned her veterinary degree from the University of Melbourne Veterinary School in 2008. After spending a year in general practice in Cairns, she moved back to Melbourne to undertake a rotating internship. In 2011, she moved to the U.S. to complete her residency in medical oncology at the University of California, Davis. She is currently enrolled in a Ph.D. program while continuing to work as a medical oncologist in the Veterinary Medical Teaching Hospital at UC Davis.



Dr. Jennifer Willcox

received her DVM from The Ohio State University in 2008, followed by a small animal rotating internship at a private practice in the Bay Area. She then pursued an oncology specialty internship at a private practice in Tampa, Florida and a fellowship performing bone marrow transplants in dogs with lymphoma at North Carolina State University. Subsequently, she stayed on at NC State to complete a medical oncology residency. She became board-certified by the American College of Veterinary Internal Medicine (oncology) in 2014. Prior to her return to the west coast in 2015, Dr. Willcox held a one-year clinical instructor



position with the University of Missouri. Her research interests include cancer imaging techniques such as positron emission tomography (PET) and clinical trials geared toward novel therapeutic/drug development.

Dr. Robert Rebhun

is an Associate Professor of Medical Oncology at the UC Davis School of Veterinary Medicine and serves as the Associate Director for the Cancer Program within the Center for Companion Animal Health. Dr. Rebhun received both his B.S. and DVM degrees from Cornell University. In 2006, he earned a Ph.D. in Cancer Biology from the University of Texas Health Science Center at Houston/M.D. Anderson Cancer Center Graduate School of Biomedical Sciences. Dr. Rebhun completed a medical oncology residency at the Animal Cancer Center at Colorado



State University. He joined UC Davis in 2008 and was awarded a K01 SERCA award from the NIH in 2011. His research is focused on comparative and translational oncology, with specific interests in metastasis and novel therapeutics. Dr. Rebhun's main areas of interest include: longevity and breed disposition to cancer, treatment of metastatic cancers, novel targeted therapeutics for cancer, comparative and translational oncology, training clinician scientists, improving quality of life for pets with cancer, improving the standard of care for patients with cancer, and identifying risks for development of cancer.

Radiation Oncology



Our Radiation Oncology Faculty

Dr. Michael Kent

earned his B.A. in Political Science from Boston University and his DVM from UC Davis in 1997. He received his Masters in Clinical Research from UC Davis in 2006. Dr. Kent also completed an internship at the University of Pennsylvania. Today, Dr. Kent is the director of the Center for Companion Animal Health. He is also co-director of the Comparative Cancer Center, co-program leader for the UC Davis Health Comprehensive Cancer Center's Comparative Oncology Program and a professor in the school's Department of Surgical and Radiological Sciences. Additionally, Dr. Kent serves as



chair of the data safety monitoring board of the National Cancer Institute's Comparative Oncology Trials Consortium. He has been involved in numerous studies of dogs and cats with cancer and has published more than 70 research papers.

Dr. Katherine Hansen

received her DVM from UC Davis School of Veterinary Medicine in 2008. She completed an internship at the University of Pennsylvania in 2009 and a post-doctoral associate position at Duke University in 2011. She returned to UC Davis for her residency in radiation oncology, which was completed in 2013, and



she has been on the faculty in radiation oncology at UC Davis ever since. She strives to maintain a high quality of life for her patients, and her primary interests are in advanced radiotherapy and palliation.

Dr. Alain Théon

received his DVM from Ecole Nationale Vétérinaire d'Alfort, (Maisons-Alfort France). Upon graduation from veterinary school Dr. Théon completed a 3-year research doctorate program in Radiation Biology at University Paris-Est (Creteil, France) concurrently with a two-year internship in Radiation Oncology at Tenon Hospital (University Medical Center in Paris, France). During this time he decided to pursue a career in veterinary radiation oncology because it fulfilled his interest in cancer research, technology and patient care. As a result, he decided to move to the U.S. to pursue a training program in veterinary radiation



oncology since none were available in France. He completed a two-year limitedstatus residency in Therapeutic Radiology at the UC Davis School of Veterinary Medicine. In order to finish a research project on the use of hyperthermia for treatment of cancer in dogs, he completed a M.S. degree in Comparative Pathology at UC Davis funded by the Center for Companion Animal Health. Although his initial plan was to go back to France, he struggled with the thought of leaving the cutting edge research and state-of-the-art technology he enjoyed at UC Davis. When a unique opportunity came in 1990, he joined the School of Veterinary Medicine faculty. Since then he has dedicated his career to teaching and research that benefits dogs, cats and horses with cancer.

Dog and Owner Help Each Other Beat Cancer



When Chance, a 12-year-old male golden retriever, was diagnosed with cancer a year ago, his owner, Lauren Patterson, knew she had to do everything she could to save him, for he had saved her a decade before when the same happened to her. Diagnosed with breast cancer in 2006, Patterson enlisted Chance to be her hero through the ordeal. He was given permission to accompany Patterson to her appointments and was a source of encouragement during her fight. While she credits her doctors with saving her, of course, Patterson doesn't dismiss the healing powers Chance held for her during that time. When she was going through chemotherapy treatments, Patterson was worried that Chance's high energy level would result in him jumping on her like he normally did. Her compromised state was not going to be able to handle his rambunctiousness. "It was remarkable," said Patterson. "I would lie down on the sofa, and he just laid next to me. He was still his high-energy self with everyone else, but with me it was different. Part of the gift of Chance is that he has been a great healer to me, which is why it was so important for me to be a great healer for him. The only way I could do that was by taking him to UC Davis."

Patterson, now in remission from her cancer, was determined to help Chance achieve the same outcome. A few months prior, the

"Dr. Théon cared about Chance so much. Without him thoroughly explaining the radiation procedure to me, it would have been very distressful for me to have Chance receive radiation."

- Lauren Patterson, client

Neurology/Neurosurgery Service performed an unrelated procedure to relieve pain in his compressed spinal column that was resulting in rear limb lameness. During that surgery, faculty member Dr. Maggie Knipe and resident Dr. Devin Ancona discovered a tumor that turned out to be an aggressive cancer. Chance underwent two more surgeries—performed by faculty member Dr. Phil Mayhew and resident Dr. Rebecca Hersh-Boyle of the Soft Tissue Surgery Service—to remove multiple tumors determined to be malignant liposarcoma and squamous cell carcinoma.

Using wide margins to remove the tumors, microscopic elements of the disease were left behind which needed radiation therapy to eradicate. "The radiation oncologists were just incredible," said Patterson. "When this happened, there were so many things to

worry about. That last thing you want is any question whatsoever in regards to the doctors who are caring for him. I trusted everyone at UC Davis in a way I've never trusted doctors."

"My trust came from three places," Patterson continued. "One, I knew I was in the best hands at UC Davis. Two, the time they spent with me and the thoroughness with which they used the diagnostic testing to inform what they were doing; their knowledge base was so current. Finally, they just really cared about Chance as a dog and me as a person. That trifecta was a huge blessing. If I would have done this closer to home, part of me would have always thought, 'I'm not giving him the best possible care because we're not at UC Davis.'

Dr. Alain Théon of the Oncology Service took the time to answer all of Patterson's questions and address her concerns about radiation. According to Patterson, the most difficult part of her cancer treatments was the radiation, much more so than the surgery or chemotherapy.



Dr. Théon explained what people experience with radiation and what dogs experience, which can be vastly different. The overwhelming majority of dogs tolerate radiation well.

"Dr. Théon cared about Chance so much," said Patterson. "Without him thoroughly explaining the radiation procedure to me, it would have been very distressful for me to have Chance receive radiation. "Chance underwent 17 rounds of radiation treatments in a 24-day period to kill any remains of the cancerous cells left after surgery. Radiation therapy is conducted on UC Davis' state-of-the-art linear accelerator. Installed nearly four years ago thanks to generous donors to the school, it remains the most advanced accelerator anywhere in veterinary medicine. Results of testing conducted at Chance's recheck appointments showed him to be cancer free. Chance's oncology treatments were made possible, in part, by a generous grant from the Blue Buffalo Foundation's support of the Petco Foundation pet cancer treatment program at the UC Davis veterinary

hospital. The grant helps support treatments for domestic companion animals suffering from cancer. The project is designed to support pet parents of modest means or pet parents whose pets provide a service to others. "When they told me Chance needed radiation, and I knew I couldn't afford it, it was a very difficult time for me because I wanted to do everything I could to help him," said Patterson. "He's got this amazing personality that he shares not just with me, but with everyone he meets. He's not just a gift for me, he's a gift for everybody." When Patterson was told that Petco was going to cover all the expenses of his radiation treatments, she was astounded. "This was the gift of life from them, and I'm so grateful."

We are grateful for the support from the Petco Foundation and Blue Buffalo Foundation to help our animal patients receive essential cancer treatments.

Surgical Oncology

"At UC Davis, we offer the highest level of clinical care, with world class equipment and specialists who have undergone extensive training. These specialists are passionate about their patients and invest themselves completely in their clinical care."

– Dr. William Culp

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GRADIANCE

Our Surgical Oncology Faculty

Dr. Philipp Mayhew

is a 1996 graduate of the University of Edinburgh. He completed his small animal surgery residency at the University of Pennsylvania, School of Veterinary Medicine in 2004, where he also completed an orthopedic research fellowship. Before joining the UC Davis faculty in 2010, Dr. Mayhew served as assistant professor of small animal surgery at the University of Pennsylvania, and worked in private practice in Washington state. He performs all types of surgery while offering particular expertise in minimally-



invasive techniques such as laparoscopy and thoracoscopy. Dr. Mayhew has published more than two dozen research papers to assess new techniques for disease treatment and advanced surgical procedures.

Dr. Michele Steffey

received her DVM from the UC Davis School of Veterinary Medicine in 1999. After graduation from veterinary school, she completed an internship at the University of Pennsylvania and then completed her residency in small animal surgery at Cornell University. Following her residency, Dr. Steffey served on the faculty at Cornell until 2007, and then joined the faculty at UC Davis. While adept in all aspects of soft tissue surgery, her areas of special clinical interest include surgical oncology, laparoscopic and thoracoscopic



surgery, and interventional radiology. She is a Diplomate of the American College of Veterinary Surgeons, and an ACVS Founding Fellow in Surgical Oncology. Dr. Steffey is a founding veterinarian and advisor to the Tails of Hope Foundation, a nonprofit organization dedicated to aiding in the fight against cancer in veterinary patients. She is active in a number of clinical and translational research projects, including the use of near-infrared fluorescent imaging in the surgical treatment of various diseases and application of minimally invasive tumor ablation in veterinary patients. She has also authored numerous scientific publications and chapters in various veterinary textbooks.

Dr. William Culp

graduated from the University of Pennsylvania, School of Veterinary Medicine. After graduation from veterinary school, he remained at the University of Pennsylvania to complete a rotating internship in small animal medicine and surgery followed by a surgical residency. Dr. Culp is board certified as a Diplomate of the American College of Veterinary Surgeons, and he has pursued additional training in cancer surgery at the Colorado State University Animal Cancer Center, during which he completed a Surgical Oncology Fellowship. Additionally,



he has completed an Interventional Radiology/Endoscopy Fellowship at the Animal Medical Center in New York City. Dr. Culp was selected as an ACVS Founding Fellow of Surgical Oncology in 2012 and an ACVS Founding Fellow of Minimally Invasive Surgery in 2017. He is currently a member of the Soft Tissue Surgery service at UC Davis. He is interested in many areas of soft tissue surgery, but his major focuses are surgical oncology and interventional radiology.

Dr. Michelle Giuffrida

graduated from the University of Pennsylvania, School of Veterinary Medicine in 2007. She completed an internship in medicine and surgery at North Carolina State University, a residency in surgery at the University of Pennsylvania, and a fellowship in oncologic surgery at the University of Florida. Dr. Giuffrida is a board-certified surgeon, holding the titles of Diplomate (Small Animal) and Fellow in Surgical Oncology through the American College of Veterinary Surgeons.



Before joining the UC Davis faculty, Dr. Giuffrida served as a lecturer in surgical oncology at Pennsylvania, and completed a M.S. in Clinical Epidemiology degree at the Perelman School of Medicine, gaining skill in the design and conduct of research studies that involve observing and treating actual patients (as opposed to experiments performed in a laboratory). Dr. Giuffrida performs all types of soft tissue surgery, while offering particular expertise in surgery for cancer patients. Her research goal is to improve the way we study diseases in pets. By developing new methods to scientifically measure symptoms, quality of life, and other outcomes that are important to pets and their families.

Clinical Trials Bringing Hope to Our Patients



With over 20 ongoing clinical trials and 384 patients enrolled in the 2016-2017 academic year, we are offering more options for previously untreatable cancers.



Oncology Clinical Trials

Teri Guerrero

is the Clinical Trials Coordinator, and she has a B.S. in Biology with a chemistry emphasis. She has worked in private practice as a veterinary assistant and office manager for ten years. She worked in the preclinical and clinical laboratory services in the pharmaceutical and biotechnology industry where she obtained her AAALAC accreditation, and gained extensive knowledge for Good Laboratory Practice (GLP) and Good Clinical Practice (GCP). For the past ten years, she has worked as a Clinical Trials Coordinator for the



UC Davis Veterinary Oncology Program running multiple clinical trials and coordinating the biorepository for tumor banking collection. She has experience working with small animals and large animals, processing tumors, normal tissue collection, serum, plasma, and whole blood, along with other processing techniques.

Frank O'Daniel

received his B.A. from Southern Illinois University in Carbondale, IL. in 1991. After a career in retail he obtained his RVT from Veterinary Allied Science Educators in Davis, CA in 2011. He worked in general practice in the San Francisco Bay area as a multi-unit hospital director and RVT Training/Recruiting Manager until 2011. He began his career at UC Davis in non-human primate research (California National Primate Research Center) as a Lead RVT/Research Associate. In 2017 he began working at the Veterinary Medical Teaching



Hospital as a Staff Research Associate/Clinical Trials Coordinator. He has held multiple clinical positions, both in research as well as surgery/anesthesia over the course of his time at UC Davis. His main areas of interest are small animal oncology and infectious disease as well as non-human primate research and how it correlates to the human model.

Dr. Chrissy Kapelewski Kinkade

received her B.S. in Biological Sciences with a concentration in Neuroscience from the University of Maryland, College Park in 2006 and her Ph.D. in Neuroscience from the Pennsylvania State University in 2010. Immediately after receiving her doctorate, she worked as a Research Compliance Analyst at UC Berkeley until 2013 when she came to UC Davis to become a Clinical Trials Analyst in the Veterinary Center for Clinical Trials.



UC Davis Osteosarcoma Clinical Trial Showing Success

Fred, a six-year-old male shepherd cross, was diagnosed by his referring veterinarian with cancer in his left forelimb in April 2016. Due to preexisting orthopedic issues, he was not a candidate for the traditional amputation and chemotherapy treatment. Faced with only being offered palliative care for Fred, his dedicated owners, Rob and Linda, continued to hope and sought out other options. They discovered a new clinical trial at the UC Davis veterinary hospital that offered a cutting-edge approach to treating dogs with osteosarcoma.

"From the first meeting, we knew Dr. Michael Kent, Teri Guerrero (oncology clinical trials coordinator), and the entire UC Davis team would take great care of Fred," Rob said.

The trial, sponsored by the National Cancer Institute (NCI) and being run in conjunction with the UC Davis School of Medicine's NCI-designated Comprehensive Cancer Center due to a special interest in its future applications to human medicine, investigates the potential of a dog's immune system to be manipulated to fight off its own cancer. After irradiating the tumor, veterinarians collect a particular type of the dog's white blood cells, known as Natural Killer (NK) cells, then stimulate and grow the cells in a laboratory before injecting them back into the dog's tumor. Ideally, lung metastasis, or the spread of the tumor to the dog's lungs (which occurs in more than 90 percent of osteosarcoma cases), will be slowed or stopped entirely by these NK cells.

Fred's treatment started with palliative radiation to help control the local disease and reduce pain as well as to create a signal to the immune

system that the NK cells could react to. He also began receiving monthly injections of zoledronate, a drug used to help prevent fractures in bones stricken with cancer. The following three weeks of radiotherapy ran seamlessly, and Fred's sweet demeanor and fuzzy, lovable appearance quickly made him popular amongst the team of veterinarians, technicians, and students in the Oncology Service who cared for him.

Following radiation therapy, Fred received the first of two intratumoral NK cell injections without any complications. During the appointment for his second NK cell injection, Dr. Kent, the lead investigator on the trial, noticed Fred's hesitation to bear weight on his left front leg. He consulted with the Orthopedic Surgery Service, and with the help of the Diagnostic Imaging Service, the team of veterinarians discovered fractures to both the radius (where the tumor was located) and the ulna, which is typical given the nature of Fred's disease. A temporary splint was put in place and the second NK cell injection was given as planned. Several days later, orthopedist Dr. Po-Yen Chou surgically repaired Fred's fractures.

By August, a CT scan revealed exciting news for both Fred and the osteosarcoma trial – there

Fred was enrolled in a new UC Davis clinical trial to treat dogs with osteosarcoma.

Clinical Trials Bring Hope to Our Patients

was no evidence of tumor spread or metastasis. Fred continued to receive zoledronate injections for two more months, and concluded his participation in the clinical trial at the end of October. His owners are thankful for the extension to Fred's life that this trial has provided.



"No matter the long-term outcome, we feel he has received the very best Dr. Michael Kent, right, and team prepare a dog for CT diagnostic imaging.

of care, and that's why we will always be grateful that UC Davis is able to offer clinical trials," Linda said. "Making decisions in the treatment for pets that have cancer is never easy, but we have absolutely no regrets, and, as pet parents, that's as good as it gets."

This trial will have wide-reaching applications in both veterinary and human medicine. Over the last few years, immunotherapy has become the fourth arm in treating cancer, along with more traditional treatments such as surgery, radiation therapy and chemotherapy. By learning how to overcome immune tolerance and immunosuppression caused by the tumor, this study and other research UC Davis is conducting on immunotherapy hope to provide oncologists more options for treating cancer in both pets and their owners.

Companion Animal Oncology Clinical Trials In-Progress

Lymphoma

- 3 canine trials
- 2 feline trials

Osteosarcoma

2 osteosarcoma trials and collection for tumor trial

Oral Melanoma

2 oral melanoma trials and collection for tumor trial

Prostate

1 prostate oncology trial

Glioma

- Collection for tumor trial
- Enrolling patients for new trial

Mast Cell Tumor

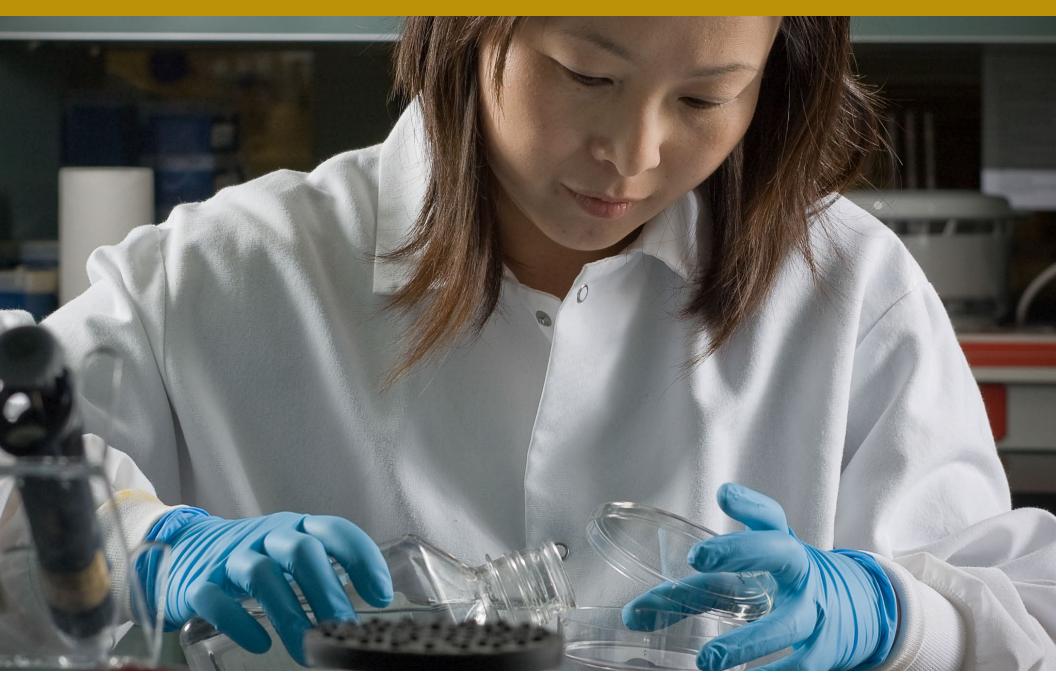
 Recently completed 1 trial and seeking FDA approval

Transitional Cell Carcinoma or Bladder Cancer

Currently surveying owners



Beating Cancer Through Research



Our Basic Science and Translational Oncology Faculty

Dr. Xinbin Chen

completed his veterinary training at Anhui Agricultural University in China and became a livestock veterinarian in 1982. He did his postgraduate study in infectious diseases at Nanjing Agricultural University and received a M.S. degree in 1985. Dr. Chen received a World Bank fellowship to study at Michigan State University and earned a Ph.D. in Microbiology in 1991. He completed postdoctoral training at Columbia University



with a fellowship from the Department of Defense (DOD) from 1992-1996. He started his career as an assistant professor at the Medical College of Georgia with a DOD career development award in 1996. He was promoted to Full Professor at the University of Alabama at Birmingham in 2004. In 2007, Dr. Chen became a Professor at UC Davis Schools of Veterinary Medicine and Medicine. He has served as Co-Leader of the Comparative Oncology Program at UC Davis Comprehensive Cancer Center and as Director of Veterinary Oncology. Since 2015, he has served as director of the Veterinary Scientist Training Program. He received the Excellence in Teaching award at the Medical College of Georgia in 2000 and the Pfizer Excellence in Research award at UC Davis in 2010. Dr. Chen is also a fellow of the American Association for the Advancement of Science.

Dr. Ellen Sparger

graduated from veterinary school at the University of Georgia in 1977, completed a small animal internship at Purdue University and then an internal medicine residency at Michigan State University. She was an internist in private practice and then was an instructor at the University of Florida. After completing a Ph.D. from the University of California, Davis in 1990 she began a research career in immunology working on retorviruses. Using her experience in feline and nonhuman primate T cell and B cell immunology she now pursues research studies in the use of



immunotherapeutic approaches for canine and feline cancer syndromes. Her ongoing studies characterize immune responses, particularly regulatory CD4 T cell and effector CD8 T cell responses, in canine and feline cancers with the intent to determine potential targets for immune manipulation in companion animal neoplastic disease. She is currently an Associate Adjunct Professor at UC Davis and has published over 30 research papers.

Dr. Luke Wittenburg

received his B.S. in Animal Science from New Mexico State University and his DVM from Colorado State University. Upon graduation from veterinary school Dr. Wittenburg completed a one year internship at a private practice in Los Angeles with strong programs in medical and radiation oncology. During this time he decided to pursue research on novel therapeutics for cancers, and he went back to Colorado State University to begin a graduate program in cancer biology. In 2010 he



received his Ph.D. in Cell and Molecular Biology with a focus on cancer biology. His research focus was on improving the effectiveness of doxorubicin in canine osteosarcoma with the use of an epigenetic modifying drug. This experience led him to ultimately pursue a residency in veterinary clinical pharmacology at Colorado State University. He became a diplomate in the American College of Veterinary Clinical Pharmacology in 2013. Afterwards, Dr. Wittenburg joined the CSU faculty for three years in the department of clinical sciences. Although he enjoyed contributing to pharmacology studies for various services within the hospital, when the opportunity came in 2016 to combine his interests in drug discovery and clinical pharmacology he joined the UC Davis School of Veterinary Medicine faculty.

Our Basic Science and Translational Oncology Faculty

Dr. Jin Zhang

received her B.S. in Biochemistry from Anhui University in China in 1997 and her M.S. in genetics from Zhejiang University in China in 2000. She earned a Ph.D. in genetics from Fudan University in China in 2003. Afterwards, Dr. Zhang completed her three-year post-doctoral training at University of Alabama at Birmingham. During her postdoctoral training, Dr. Zhang's research focus was on the tumor suppressor p53, the most common mutated gene in human and companion animal tumors. In 2007,



Dr. Zhang was appointed as an Assistant Project Scientist in the Department of Surgical Radiological Sciences at UC Davis and was promoted to an Assistant Researcher in 2015. Dr. Zhang has been involved in many cancerrelated studies in both human and companion animals and has published more than 40 research papers.

Dr. Peter Dickinson

graduated from Liverpool University Veterinary School in 1989. Following one-year in mixed general practice he completed a two-year surgery/anesthesia internship at Glasgow University Veterinary School. He received his Ph.D. in developmental neuroscience in 1995, also at Glasgow University, before completing a Neurology/Neurosurgery residency at the University of California, Davis in 2000. He is currently Professor of Neurology/Neurosurgery at the UC Davis School of Veterinary Medicine



and is a diplomate of the American College of Veterinary Medicine (Neurology). His clinical and research interest has been in the field of neuro-oncology and he is director of the Petersen Foundation Brain Tumor Laboratory. "A career in academia allows me to do all the things I love in this profession. I love seeing patients and working with their care-givers. I get to conduct research that will hopefully improve cancer treatments and cancer survival for pets. And maybe one day even people too! UC Davis is an amazing place to be a veterinary oncologist."

– Dr. Jenna Burton

Dr. Danika Bannasch

earned her DVM degree from the UC Davis School of Veterinary Medicine and her Ph.D. in mouse molecular genetics at Princeton University. She is currently a professor in the Department of Population Health and Reproduction in the UC Davis School of Veterinary Medicine and is the first faculty member to hold the prestigious Maxine Adler Endowed Chair in Genetics. An accomplished veterinary geneticist, Dr. Bannasch focuses her research on the identification of the molecular causes of inherited diseases in dogs and horses. Her laboratory has identified the DNA changes responsible for Lethal White Foal Syndrome, Hereditary Equine Regional



Dermal Asthenia, Hyperuricosuria, Alaskan Husky Encephalopathy, Cleft palate, Cleft lip and palate, Spinal Dysraphism, Glioma susceptibility, Chondrodystrophy and Saluki Spongiosis. Important research findings have also led to animal models used for similar human diseases. By studying naturally occurring diseases in animals, the Bannasch Laboratory is discovering a triad of significant advances: the development of diagnostic tests to aid animal breeders; the identification of novel genes and pathways as candidates for human disease; and an understanding of basic molecular mechanisms of disease. Dr. Bannasch also breeds Nova Scotia Duck Tolling Retrievers under the Aqueus kennel name. She is active in conformation, agility and hunt tests with her dogs. She has owned and bred over 20 champions and numerous agility and hunt test titled dogs including four champion Master Hunters!

Our Basic Science and Translational Oncology Scientists

Dr. Fernando Alegre

graduated with honors in Veterinary Medicine in 2010 and obtained M.S. in Health Science Research: Specialty Veterinary in 2011 from the University of Extremadura in his home city of Caceres, Spain. He received his Ph.D. in Physiology/Pharmacology in 2017 from the University of Valencia, with a focus on liver toxicity of HIV drugs. His research was focused on the involvement of mitochondria, autophagy and



fibrogenic/inflammatory responses in the adverse effects produced by Efavirenz, one of the most widely used anti-HIV drugs. He joined Dr. Luke Wittenburg's lab in 2017 to identify novel targets and therapeutics for osteosarcoma.

Dr. Daniel York

After completing an undergraduate degree in neuroscience at Manhattanville College in New York, he spent two years in drug discovery research at a Bay Area biotech company with a focus on oncology. Dr. York brought that experience UC Davis in 2006 where he continued research in veterinary



neuro-oncology as a staff research associate. In 2013, he received his doctoral degree from the Comparative Pathology graduate program at UC Davis. He is currently an assistant project scientist in the Comparative Oncology Lab in the Center for Companion Animal Health where he provides research and management support to several oncology projects and clinical trials. His research focuses on molecular mechanisms involved in tumorigenesis and metastasis and the genetic and epigenetic factors that pre-dispose some dog breeds to certain cancers, including osteosarcomas, melanomas, and gliomas. Through a better understanding of these oncogenic mechanisms, novel therapeutics can be identified and evaluated for companion animals.

Dr. Jin Wook Choi

completed his B.S. degree at Hanyang University in Seoul, South Korea and went on to receive his M.S. and Ph.D. degrees from the University of California, Irvine. He has studied metabolic engineering with research focused on the production of drug precursors from microorganisms. Now, as a post-doctoral researcher, he is developing therapeutic antibodies to treat canine cancer focusing on immunotherapy approaches.

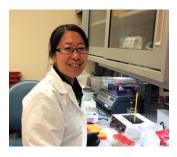
Ms. Kellie Snider

received her B.S. in Animal Science from California Polytechnic State University, San Luis Obispo. During her last two years at Cal Poly, Kellie worked in an animal nutrition lab on campus where she first discovered an interest in research. After graduation, she stayed in San Luis Obispo to work at a veterinary practice as a vet assistant and boarding manager for two years before accepting admission to the UC Davis School of Veterinary Medicine. During her first year at UC Davis, Kellie applied for the STAR summer program offered through the veterinary school to gain experience in oncology research. She discovered the ideal opportunity working in Dr. Wittenburg's lab

where her STAR research project investigated the therapeutic potential of a MicroRNA-34a prodrug for canine osteosarcoma. She enjoyed the experience so much that she officially joined the lab upon completion of the summer program.

Dr. Hong Chang

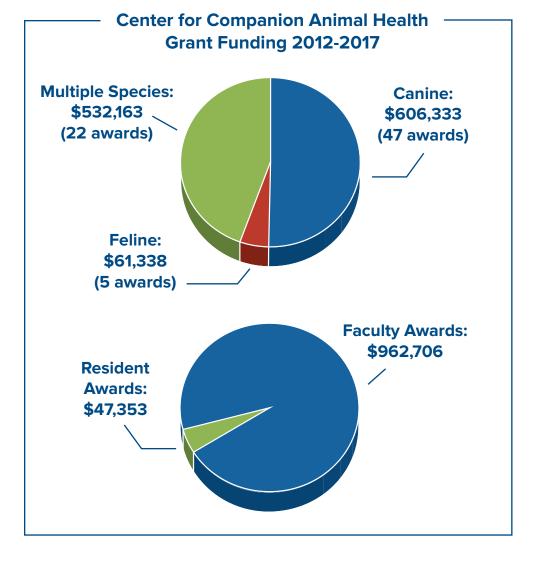
earned her B.A. in Biotechnology in 1997 and M.A. in Basic Veterinary Medicine in 2001 at Northeast Agricultural University in China. She also received her Ph.D. in Genetics from UC Davis in 2006. She completed post-doctoral training in biotech industries and at the UC Davis School of Medicine (2007-2011). Dr. Chang has been working in Dr. Michael Kent's laboratory at the UC Davis School of Veterinary Medicine since 2011.



The CCAH provides grant funding on a competitive basis to faculty for studies dedicated to advancing the health of dogs, cats and exotic pets. Since 2010, the CCAH has awarded nearly \$3 million to support faculty research. In 2016-17, the CCAH funded 36 faculty grants totaling nearly \$489,000, 6 matching grants in the amount of \$43,900, 17 equipment grants for \$275,900 and 12 resident research grants totaling \$48,420.



Institutional Support for Research



Grants Enhance our Research Efforts

Extramural Funding:

Dr. Jenna Burton: 5 grants = \$495,700

- 1. Preclinical comparison of three indenoisoquinolines candidates in tumorbearing dogs
- 2. A multicenter, randomized, placebo-controlled study of AT-005 in combination with CCNU chemotherapy in the treatment of canine high grade, peripheral T-cell lymphoma
- 3. Evaluation of orally-administered mTOR inhibitor rapamycin in dogs with osteosarcoma
- 4. A contemporaneous controlled study of the standard of care (SOC) in dogs with appendicular osteosarcoma
- 5. Evaluation of orally-administered mTOR inhibitor rapamycin in dogs in the adjuvant setting with osteosarcoma

Dr. Xinbin Chen: 10 grants = \$2,943,700

- 1. Mechanism of p73 dependent tumor suppression (multiple awards)
- 2. Regulation of mutant p53 expression and oncogenic activity (multiple awards)
- 3. Mechanism of p53-dependent tumor suppression (multiple awards)
- 4. The role of DNA polymerase eta in DNA damage response and p53 activation
- 5. The Role of the p63-RBM38 loop in tumor supression

Dr. Michael Kent: 2 grants = \$1,229,199

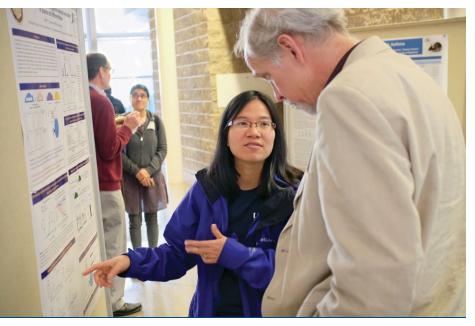
- 1. Development of PET imaging biomarkers to predict enhanced radiotherapy by a novel H-NOX oxygen carrier in glioblastoma
- 2. Use of a novel oxygen carrier and immune responses in dogs treated with radiotherapy for canine malignant melanoma

Dr. Robert Rebhun: 3 grants = \$1,305,456

- Enhancing natural killer immunotherapy with first-in-dog trials of inhaled recombinant IL-15 and super-agonist IL-15 in naturally occurring canine cancers
- 2. The relationship between epidermal growth factor receptor and hedgehog signaling (multiple awards)

Dr. Katherine Skorupski: 1 grant = \$51,600

 Phase 3 study to compare efficacy and safety of masitinib to placebo in the treatment of grade 2-3 non-resectable mast cell tumors in dogs not previously treated by chemotherapy (other than corticosteroids) or radiotherapy

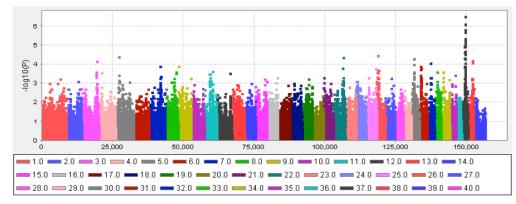


"I chose to work in the School of Veterinary Medicine at UC Davis because of the strong background in research and innovation in veterinary medicine as evidenced by Drs. Kent and Chen. I believe that our studies in veterinary oncology can improve the quality of life of both animals and owners in the future."

– Dr. Fernando Alegre

In the Pipeline: Longevity and Golden Retrievers

There appears to be a gene associated with longevity in golden retrievers. This gene may be associated with the development of cancer. Work is ongoing to determine the gene and sequence that appears with long-lived golden retrievers. If successful, this work could lead to identification of a gene which could be selected for/against to improve lifespan in golden retrievers. We are now expanding this study into other breeds.



Longevity

A "Manhattan-plot" showing areas of the genome that differ among long-lived golden retrievers



Creating Impact and Spreading Knowledge

OPLOS ON

A representation of research publications produced between 2015-2017, with many more to come

Exotic Animals

NICHBELS. KETT, MAL DVM, DACVM (Shoalogy, DACVK Kalaa

Radiation therapy Small mammal

TRODUCTION

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PROSPECTIVE COMPARISON OF TUMOR STAGING USING COMPUTED TOMOGRAPHY VIRSUS MACINITIC RISONANCE IMAGING FRNDINGS IN DOKIM TIN MAAL NIOVLASIA: A PILOT STUDY

CAME N. LON, WILLIAM T. N. CULP, LYNELER, R. DODONY, MICHAEL KENT, PHILIP MATHE Lan A. DANNEY, ALANA CARR, SARAI POCHASI

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	an tamor volume which was IR-P5 higher than CT imaging. Disagreement between CT and MRI
	with meningeal enhancement, in which two dogs were positive for meningeal enhancement on MRI
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Area:

Radiation and Exotic Animal Species

Impact:

Little is known about treating cancer in exotic animal species. This review paper is the most extensive review to date compiling all knowledge known on treating birds, small mammals, reptiles and fish with radiation therapy for the treatment of cancer.

-	BMT1 15 Expressed in Canine Osteosarcoma and Contributes to Cell Growth and Chemotherapy Resistance Meditypited ¹⁵ State Vel ¹⁵ , Resistance Causes ¹ , State Materi, ¹⁵
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Area:

Osteosarcoma, Stem Cells and Chemotherapy Resistance

Impact:

Failure of cancer therapies occurs because not all cells are sensitive to therapy. A subset of cancer cells termed 'cancer stem cells' are believed to be resistant to traditional therapies and may lead to treatment failures. It was determined that a cancer stem cell signaling pathway (BMI-1) was active in canine bone cancer cells. We also found that this pathway could be inhibited in canine tumor cells using an inhibitor developed against human BMI-1. We also showed that this inhibitor sensitizes tumor cells to chemotherapy induced killing. We are now expanding studies into canine brain tumors and tumors of the mammary gland.

Area:

Imaging and Nasal Tumors

Impact:

The current best practice for imaging nasal tumors in dogs is done using CT scans. This is largely done as CTs are more widely available than MRI, are easier and shorter to perform and CTs are needed for planning radiation therapy. In general MRI gives better soft tissue definition than CT scans. This prospective pilot study showed that while CT was very good for estimating bone involvement MRI was superior in identifying tumor margins and also cases where there was tumor extending into the brain. While this does not change how we will practice for most cases, in those with some evidence of bone destruction we can use MRI to better determine the extent of the tumor into surrounding tissues and combine imaging techniques to allow for better treatment planning.



dogs (15% compared to (25%) $P \sim 200$). Furthermore, investigation (25%) and interpland association of the single of the social structure of the soci

Deeps againform advances in anti-mark drug therapy, chemotherapy, advands insure on animating CRNS's results on Againform publics in advanced and the advances of the advances of the advances durating site effects of chemotherapy and stareful constraints or pointer one completences, transmomerations, and poor mathicand datas, CRNV is retrained produced by the advances of the durating of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances duration of the advances of the advances of the advances of the advances duration of the advances of the advances of the advances of the advances duration of the advances of the advances of the advances of the advances duration of the advances of the	Indelling discuption of the Modelheits hunter, discipline is generatives: and exception of the discipline is in presentability, indices, Addres of Computitive Web 8. B. Millen, Yunner Melder, Theor, Hand Anger, Printer, Hallen, Kunner J. Galdini, Kun, Tano O, Tanada Anger, Printer Dei Como 1, Generative and Halls, Salar Venner, Holman M. 2018; D. BERCH, 2018, and S. Mark, Salar Venner, House, March M. 2018, and M. 2018, and M. 2018, and Web 1, Salar M. 2018, and M. 2018, and M. 2018, and Mark M. 2018, and M. 2018, and M. 2018, and M. 2018, and Mark M. 2018, pp. 1120–1131, and M. 2018, https://dx.2018.01.0011 Mark M. 2018, pp. 12018, pp. 12018, and Mark M. 2018, https://dx.2018.01116. https://dx.2018.01116.pp. 2018, pp. 2018
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Area:

Lymphoma and Decreasing Chemotherapy Toxicity

Impact:

Quality of life for our patients with cancer is paramount. The majority of dogs do not experience side effects from chemotherapy, however up to 40% of dogs can develop gastrointestinal side effects including vomiting, diarrhea, and inappetence. There is some experimental data in the literature that suggests fasted animals may have less side effects if given chemotherapy but this has never been tested in clinical patients. We performed a randomized, prospective study to determine whether timing of meals might influence side effects of chemotherapy. We found that skipping the morning meal before doxorubicin chemotherapy greatly reduced the incidence of vomiting in dogs undergoing chemotherapy. This is one new tool that can be used to combat side effects should they occur.

A Better Way to Treat Lung Tumors?

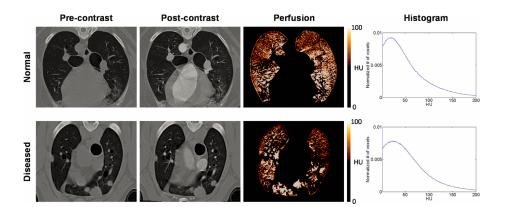
Single-energy computed tomography-based pulmonary perfusion imaging: proof-of-principle in a canine model



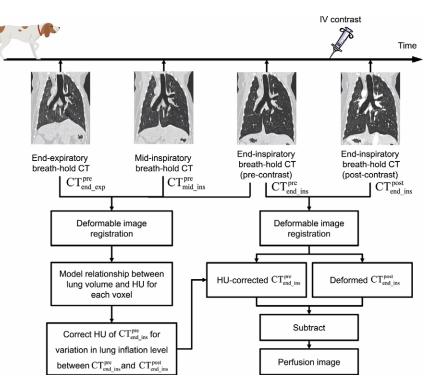
This clinical trial in dogs was a pilot to a personalized medicine approach to develop a technique to allow determination of lung that differ between perfusion and ventilation allowing for decrease toxicity associated with lung tumor radiotherapy.

The method developed can be done on a conventional CT scanner, allowing easy adoption of this technique as it develops.

This collaboration was between the UC Davis School of Veterinary Medicine oncology and radiology services and the UC Davis School of Medicine radiology department and the UC Davis NCI-Designated Comprehensive Cancer Center medical physics section of radiation oncology.



The image above shows CT scans of a dog with normal lungs and a dog with lung cancer on the bottom, along with a perfusion map showing areas where there is good blood flow and air moving as well as areas where they are misaligned, meaning areas of the lung that are not as functional. This could allow us to direct radiation treatment beams through these less functional areas and spare normal areas of the lung.



Special note:

This paper was published in Medical Physics and received the Editor's Choice column for the Medical Physics Scitation and medphys.orgwebsites - the editors select the four highest quality papers in terms of potential scientific impact and reader interest for this honor. This publication was featured in medicalphysicsweb, a publication of the UK Institute of Physics.

Targeting the Previously Untreatable with Immunotherapy



Area:

Melanoma and Immunotherapy

Impact:

This study represented a collaboration between the veterinary and medical schools using a new immunotherapy combination to treat advanced metastatic disease. We discovered a rebound immunosuppression induced by tumors helping them evade the immune system. When Krista DeZerega-Thomson and her family learned that Rohan, their beloved Labrador retriever, had melanoma — an aggressive cancer that affects both people and dogs — their hearts fell. Because it had already spread to Rohan's lungs and lymph nodes, their veterinarian told them that with no conventional treatment options available, he likely had only two more months to live.

Then the vet mentioned that Dr. Michael Kent, a professor of radiation oncology in surgical and radiological sciences at the UC Davis School of Veterinary Medicine, was conducting a unique clinical trial to treat cancers like Rohan's. Kent, director of the UC Davis Center for Companion Animal Health, remembers Rohan as a perfect candidate for the trial, part of a remarkable collaboration with Dr. Arta Monjazeb, associate professor of radiation oncology at the UC Davis Comprehensive Cancer Center.

"We are addressing the most challenging presentation in cancer medicine: a tumor that has already metastasized," says Kent. "The Cancer Center-Vet Med partnership is a great strategy to simultaneously advance treatments for animals and humans."

Blending radiation with immunotherapy

The novel treatment approach blends radiation and immune therapies to break up the cancer, then stimulate a dog's or a person's own defenses to recognize the tumor fragments as foreign and mount an attack to destroy them. According to Monjazeb, it effectively helps create an individualized vaccine against the cancer.

"Marrying radiotherapy with immunology is bringing about a revolution in cancer therapy. Based on advances we are seeing now, we should be able to effectively treat patients who were previously considered incurable." Monjazeb has been fascinated with immunology since he participated in research as an undergraduate at UC Berkeley. During medical school he also obtained a Ph.D. in cancer biology, focusing on the role of inflammation and immunology in cancer. After medical school he specialized in radiation oncology. His interest in the role of the immune system in human disease continued, and he performed a research fellowship in cancer immunotherapy.

At the Center for Companion Animal Health in Davis, Rohan underwent four radiation treatments aimed at his tumor and lymph nodes. Radiation therapy on its own has many immunological effects, Monjazeb explains. For one, it kills tumor cells, making them more recognizable by the person's immune system. Dying cancer cells release a surge of proteins that activate the host's immune defenses, which generate cancer-specific white blood cells to fight the cancer. Secondly, radiation breaks up the tumor, allowing the body's circulating immune cells in the blood to gain better access to the remaining tumor. In addition, radiation destroys immune-suppressive cells recruited by the cancer that have kept the host's immune system at bay.

In addition to giving him radiation treatments, veterinarians injected immune-enhancing drugs into Rohan's tumor site to stimulate his immune system to mount a local response to the tumor.

At home in between treatments, Rohan received oral drugs that helped stop the immune suppression caused by his tumor. The drugs put a damper on regulatory T-cells that normally lower the body's immune response — a safeguard that keeps our immune system from recognizing our body as foreign, but also hampers fighting a tumor.

Targeting the Previously Untreatable with Immunotherapy

"The combination of radio-therapy and immunotherapies is like putting one foot on the gas and taking the other off the brake at the same time," says Monjazeb. "This strategy promotes a maximal response against the cancer."

Both Kent and Monjazeb were very pleased with how Rohan and the other dogs in the trial responded to the unique therapy. Rohan lived another six months, three times longer than had been predicted without therapy. And, as importantly, his quality of life remained good throughout the treatment.

"Every time he came out of treatment, he had more energy," recalls DeZerega-Thomson, whose family includes her husband and two children, ages 8 and 10. "We took him to the lake and hiking — he really enjoyed his last months."

Dogs as models

Monjazeb notes that dogs make excellent experimental models for human cancers, and that the collaboration with the veterinary school has allowed him to rapidly advance his research. Spontaneous cancers in dogs behave much more like those in humans than do cancers induced in lab mice, he explains. This makes results from dog trials much more likely to predict outcomes in people with cancer. The fact that dogs with such advanced disease responded so well to even a short course of therapy is extremely encouraging, and he hopes to soon begin safety trials in human patients who have metastatic melanoma.

> "Partnerships of this kind can be done only at UC Davis, where there is strong medical and veterinary clinical research on people and animals being done in such close proximity," Monjazeb says. "I know of no other place in the country that provides this opportunity."

> > Kent agrees, and looks forward



"It was a privilege to participate in research that not only helped Rohan, but might one day also help others — pets, as well as people."

– Krista DeZerega-Thomson, Rohan's 'mom'

to collaborating more often with the Comprehensive Cancer Center. He emphasizes that clinical trials for pets carry similar ethical concerns and require safeguards similar to those for humans.

"Research in companion animals must not diminish quality of life," he says. "Treatments must be safe, and they must not cause harm."

When Rohan did poorly several months after finishing his treatment, and it was clear that the cancer had spread throughout his lungs, everyone agreed that it was time to let him go.

DeZerega-Thomson relates how as soon as they realized that Rohan would not survive much longer, Kent met the family outdoors, where Rohan was happiest, and very peacefully put him to sleep.

"We would definitely do it all again," says DeZerega-Thomson. "It was a privilege to participate in research that not only helped Rohan, but might one day also help others — pets, as well as people."

Dr. Arta Monjazeb, Teri Guerrero and Dr. Michael Kent

Research Publications – Creating Impact and Spreading Knowledge

Original Article

Evaluation of optimal water fluoridation on the incidence and skeletal distribution of naturally arising osteosarcoma in pet dogs

R. R. Robbini, P. H. Kawi, M. S. Kenel, K. D. Watsowi, S. S. Willners, W. T. N. Cally and A. M. King, "Un-Comparative build above and clients for Comparison Actional Halds, Department of Haughed "Department of Hyndrics Halds and Haldware and the Haldware Barter and "Department of Hyndrics Haldware and Haldware and the Haldware Barter and Comparative Comparison in Haldware and Arter and Arter and The Arter and Arter and Arter and Arter and Arter and Comparative Conference on Haldware and Arter and Arter and Department of Conference Arter and Arter an

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2014 July Why & Security

Osteosarcoma Development

Impact:

Area:

We know that both genetics and environmental exposures can have effects on the incidence of cancer in people. Certain dog breeds are more susceptible to specific cancers and we are looking at this in our genetic longevity studies. Very little is known about whether any environmental exposures may be associated with cancer in dogs (some indicate that second-hand smoke, asbestos, herbicides, etc. may play a role). Several previous studies indicated that the addition of fluoride in the drinking water (done to reduce dental cavities in developed countries) may be associated with development of bone cancer in people and also in experimental animals. This is extremely controversial and many of the studies had serious flaws. We therefore compared the incidence of bone cancer in dogs presenting to the VMTH from areas that added fluoride vs. areas that did not. We found no association between bone cancer and fluoridated drinking water. This work examined both the incidence and location of bone cancer in dogs, demonstrating that this exposure is unlikely to be playing a role in development of this disease.

HHS Public Access Author manuscript J Cell Biochess. Author manuscript, available in PMC 2

J Cell Bicchem. 2012 March ; 113(3): 773-783. doi:10.1002/jcb.23403.

A Stystem Biology Approach to Identify Molecular Pathways Altered by HADC (Molebiani on Catocancence Una N. Weinder^{10,1}, Anny A. Panya, J. Annya, J. Annya

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Area:

Osteosarcoma and Drug Development

Impact:

We performed the first gene expression microarray analysis of canine osteosarcoma cells treated with an HDAC inhibitor. Further, we identified the molecular mechanisms for the anti-tumor effects that are seen with valproic acid in osteosarcoma cells, finding that changes in the oxidative phosphorylation pathway and the proteasome pathway explain some of the effects of HDAC inhibition. We also demonstrated that combinations of HDAC inhibitors and proteasome inhibitors may provide synergistic antitumor activity.

evaluation of combinati and doxorubicin treatm	nd pharmacodynamic ion hydroxychloroquine nent in pet dogs treated occurring lymphoma
Rebecca A Barnard, ¹ Luke A Wittenburg, ¹ Ravi K Amaravadi, ² D	aniel L Gustafson," Andrew Thorburn," and Douglas H Thamm ¹⁴
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NIH Public Access

Spontaneous Cancer

ublished in final oddod farm as: Clin Cancer Acz. 2010 October 1; 16(19): 4832–4842. doi:10.1158/14

Phase I Pharmacokinetic and Pharmacodynamic Evaluation of Combined Valproic Acid/Doxorubicin Treatment in Dogs with

²Call and Molecular Biology Graduate Program, Colorado State University Animal Cancer Cente 300 W. Drake Rd., Fort Coline, CO 80525 1820

¹University of Colorado Comprehensive Cancer Center, Anschutz Medical Campus, 13001 E. 17¹⁰ PL, PO Box 6511, Mal Step F434, Aerora, CO 80045

Luke A. Wittenburg^{1,2}, Daniel L. Gustafson^{1,2,3}, and Douglas H. Thamm^{1,2,3} Animal Cancer Center, Department of Cinical Sciences, Colorado State University / Center, 300 W. Drake Rd., Fort Collins, CO 80523-1520

Area: Lymphoma

Impact:

We described the first canine clinical trial that evaluated the effect of autophagy inhibition in canine cancer as a potential therapeutic option. We demonstrate that the antimalarial drug hydroxychloroquine can effectively block the autophagy pathway in canine blood cells and tumor tissue. We demonstrate that tumor tissues accumulate hydroxychloroguine at 100x the concentration seen in blood. We demonstrate that hydroxychloroquine does not alter the pharmacokinetics of doxorubicin in canine patients and provides a comparable overall response rate, even with a lower dose of doxorubicin administered.

Area:

Chemotherapy and Drug Development

Impact:

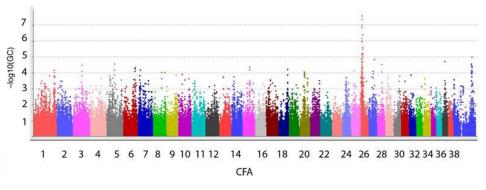
We described the first phase I pharmacokinetic and pharmacodynamic study of a combination of valproic acid and doxorubicin in spontaneously occurring cancers in dogs, a model that, for some tumor types, closely recapitulates the setting encountered in human clinical trials. Our study shows that valproic acid can be safely administered at biologically active doses with only mild side effects and does not alter the pharmacokinetics of doxorubicin. We have developed the pharmacokinetic and pharmacodynamic tools necessary for future efficacy studies of novel HDAC inhibitor-containing combinations in dog cancer patients providing the potential for better informed human clinical trial decisions.

Sometimes a trip to the water cooler delivers more than a refreshing drink—it can also lead to productive research collaborations that shed light on topics of critical concern to animals and humans. Dr. Danika Bannasch, the Maxine Adler Endowed Chair in Genetics, recalls numerous impromptu discussions in the hallways of the Center for Companion Animal Health (CCAH) with Dr. Peter Dickinson, a veterinary neurologist. For decades, he'd been puzzled with why he saw a higher incidence of gliomas among specific dog breeds, particularly in brachycephalic canines such as boxers, bulldogs and Boston terriers.

"What is it about brachycephaly and gliomas?" Bannasch recalls him asking her. "You're the geneticist—why don't you find out!"

Bannasch and Dickinson joined a team with two Swedish scientists that used genome mapping across 25 dog breeds to identify three candidate genes associated with glioma development in canines. The study, published in PLoS Genetics, may provide insights into how these often-untreatable brain tumors form in dogs and possibly in humans.

A second breakthrough concerning gliomas in dogs came a few months later and provided further definition of the candidate genes while suggesting a common pathway in dogs and humans. The research team, led by Dickinson, also included Drs. Dan York, Robert Higgins, Richard LeCouteur, Bannasch and researcher Nikhil Joshi. Results appeared in the Journal of Neuropathology & Experimental Neurology. The study was supported by donors to the CCAH,



39 cases of dogs with glioma, 141 controls across 25 dog breeds

UC Davis, The Paul and Borghild T. Petersen Foundation and the Maxine Adler Endowment.

"Cancer is cancer," says Dickinson, who has spent the past 17 years researching gliomas in dogs and pursuing a canine model to develop transitional therapies in humans. "The big pathways altered in humans are likely to be altered in dogs as well. The details may vary but it's likely to be the same big picture overall, so it's smart to use dogs as a model to identify potential genes for gliomas in humans."

Because spontaneous gliomas are the most common form of malignant primary brain tumors in humans and occur at a similar frequency in canines, human neuro-oncologists have been interested in the association of gliomas in dogs and humans for a long time. Until recently, they didn't have the tools to answer the questions of whether there were particular genes associated with the tumors in both species.

"Now we have the tools for meaningful clinical translation," Dickinson says. "With advanced imaging and treatment equipment in a veterinary hospital setting, we can almost recapitulate what doctors do for humans in dogs."

He is particularly interested in one of the three candidate genes identified, P2RX7, which is involved in immunity in the brain and may be a target for future therapeutic action.

"We've shown association, now we need to prove causation," Dickinson said. "Can we show that the genes we've identified are really responsible for the increased incidence of tumor formation in specific dog breeds?"

Evaluation of Doxorubicin-Loaded Micelles in Dogs with Non-Hodgkin Lymphoma

Dr. Jenna Burton, Primary Investigator

My main research focus at this time is the evaluation of a nanomicelle formulation of doxorubicin, which is a widely used chemotherapy drug in people, dogs and cats with cancer. Nanoparticle formulations of chemotherapy are of interest as they can lessen toxicity that occurs with conventional chemotherapy as well as accumulate in the tumor in greater concentrations through a process called enhanced permeation and retention (EPR) and through constructing the nanoparticle with tumor targeting ligands. The nanoformulation that we are investigating, DOX-DCM, was developed by collaborators at the UC Davis School of Veterinary Medicine in the laboratory of Dr. Kit Lam. Dr. Lam and his team have demonstrated that DOX-DCM has improved tumor efficacy and tumor concentration of the drug with reduced side effects as compared to standard doxorubicin in rodent models of cancer. We are interested in gaining further information regarding tolerability, biodistribution and tumor accumulation of DOX-DCM and currently have an active veterinary clinical trial evaluating the safety, tolerability and efficacy of DOX-DCM in companion dogs with lymphoma. As doxorubicin is a commonly used drug in the treatment of canine

lymphoma, we are also able to gain preliminary efficacy information in this study. This work has been supported by a UC Davis Comprehensive Cancer Center Collaborative Institutional Research Grant and my UC Davis K12 Paul Calabresi Clinical Oncology Career Development Award.

The first eight days of the clinical trial are time intensive with four visits to the VMTH and multiple blood sample collections on the 1st day of treatment for a 24 hour pharmacokinetic (PK) curve; the additional support of a second oncology clinical trials coordinator has been invaluable in completion of this work without disruption of other on-going oncology clinical trials. Our preliminary results of our DOX-DCM clinical trial in dogs with lymphoma has demonstrated a reduction of in severity and frequency of side effects typically seen with standard doxorubicin which has allowed us to escalate the dose of DOX-DCM beyond what is normally tolerable for standard doxorubicin. While efficacy is not a primary endpoint for this study, we are encouraged to see that 73% of dogs enrolled in this clinical trial have had a response to treatment.

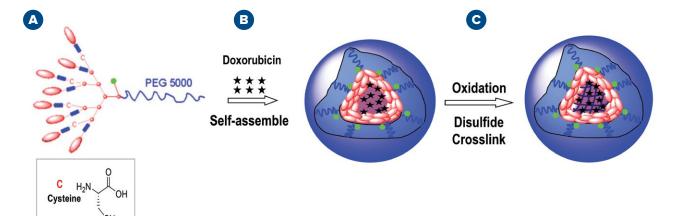


Figure 1.

Schematic of disulfide cross linked micellar doxorubicin nanoparticle (DOX-DCM). Nanomicelles are comprised of a) PEG-oliogocholic acid based telodendrimers which then b) self assemble around doxorubicin and are c) stabilized with disulfide cross-linking.

"...73% of dogs enrolled in this clinical trial have had a response to treatment."

– Dr. Jenna Burton

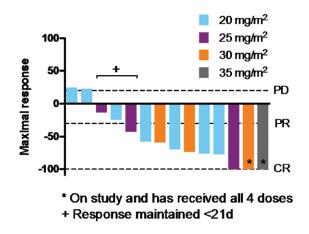
Evaluating the PK properties (i.e. what the body does to the drug) has been an important aspect of this investigation and we are fortunate to have Dr. Luke Wittenburg to help us analyze and model the PK data we have generated in this clinical trial. Preliminary results also suggest DOX-DCM has an improved PK profile as compared to standard doxorubicin and the longer terminal half-life of the drug may be part of the reason for the encouraging tumor responses we are observing. A second phase of the study will evaluate the EPR effects of DOX-DCM compared equivalent doses of standard doxorubicin.

Based on the preliminary results of this study, we are submitting an R21 application in February, 2018 to the NCI to evaluate DOX-DCM combined with a lymphoma targeting ligand, LLP2A which has been previously shown to be over-expressed and constitutively active in human and canine lymphoma cells. We will again look at this nanoparticle formulation in dogs with lymphoma and the goals of this proposal are similar as outlined above: to assess DOX-DCM-LLP2A biodistribution in the blood and tumor after administration and determine the maximally-tolerated dose and safety and to gain insight into the preliminary efficacy into this drug. If funded, the results of the this R21 proposal will be used to inform decisions to submit an application to the FDA for an Investigational New Drug (IND) for future human application or an Investigational New Animal Drug (INAD) to move forward with development of DOX-DCM-LLP2A as a new lymphoma drug for dogs.

In addition to the work described above, I also have a pending clinical trial to evaluate a nanoparticle formulation of vinblastine, a drug used for invasive bladder cancer in people and dogs, that has been decorated with a ligand that targets bladder tumors in both species. This work has been led by Dr. Chong-Xian Pan, a collaborator at the UC Davis School of Medicine, and this work is funded by a grant from the Department of Veterans Affairs.

Since 2015, I have facilitated UC Davis' continued participation in the multi-

center NCI/COP/Comparative Oncology Trials Consortium and been the site PI for three COTC trials funded by the Morris Animal Foundation (COTC020: Evaluation of Orally Administered mTOR inhibitor Rapamycin in Dogs with Osteosarcoma; COTC021: Orally Administered Rapamycin in the Adjuvant Setting for Dogs with Osteosarcoma; COTC022: A Contemporaneous Controlled Study of the Standard of Care (SOC) in dogs with Appendicular Osteosarcoma). Additionally, I was the PI and medical supervisor for the multiinstitutional COTC007b (Preclinical Comparison of Three Indenoisoguinolones) sponsored by the National Cancer Institute; results of this study are planned to be published in 2018. I have also been investigating pharmacokinetics of a commonly used chemotherapy drug in cats, chlorambucil, which is supported through a grant from the Center for Companion Animal Health. Despite its wide use in the for treatment of small cell lymphoma in cats, the PK properties of this drug have never been assessed in this species and may provide important information regarding the variability in tolerability and tumor response that is seen in the clinics. Dr. Luke Wittenburg is assisting with the PK analysis and modeling for this clinical trial. Results of this study will be then used to evaluate compounded formulations of chlorambucil to determine if differences exist between these compounded formulations and the FDA-approved versions.



Research Publications – Creating Impact and Spreading Knowledge

NIH Public Access

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histone deacetylase inhibitor valproic acid sensitizes hum d canine osteosarcoma to doxorubicin

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Area:

Osteosarcoma

Impact:

We demonstrated that the anticonvulsant drug valproic acid acts as an inhibitor of histone deacetylase activity in canine and human osteosarcoma cells providing the rationale for addition of HDAC inhibitors to current protocols for the treatment of OS. We further described the first phase I pharmacokinetic and pharmacodynamic study of a combination of valproic acid and doxorubicin in spontaneously occurring cancers in dogs. Our study showed that valproic acid can be safely administered at biologically active doses with only mild side effects and does not alter the pharmacokinetics of doxorubicin.

Evidentiation of outcome and prognostic factors of outcomes and prognostic factors of outcomes and the second seco



Area:

Osteosarcoma

Impact:

In this multicenter study we examined dogs with osteosarcoma who survived longer than the average dog to try to find prognostic factors for long term survival. Dogs with an initial diagnosis of osteosarcoma that lived more than one year had a median survival time beyond the initial year of approximately 8 months. This study found that dogs who had a limb sparing surgery site which became infected lived longer than those that had no infection. This is one of several studies that prompted Dr. Rebhun to look at the antibiotic used to treat these infections.

Area:

Chemotherapy

Impact:

We developed a method for prediction of total systemic exposure to doxorubicin in dogs using only three blood samples collected within the first hour after drug administration. This provides the ability to utilize this model in future studies that identify correlations between exposure and effects such as tumor response or toxicity while minimizing impact on our patients by limiting blood draws. INTER- AND INTRAFRACTION MOTION FOR STEREOTACTIC RADIOSURGERY IN DOGS AND CATS USING A MODIFIED BRAINLAB FRAMELESS STEREOTACTIC MASK SYSTEM

SONIA DEFENCIA, ALLINON ZWISOLOMBINOR, KATHRENE HANNEN, IAAMILLA PUUPU Alaini Thilon, Michael S Kent





Area:

Stereotactic Radiosurgery

Impact:

Precise and accurate patient positioning is necessary when doing stereotactic radiosurgery to ensure adequate dosing to the tumor and sparing of normal tissues. This study was the first to validate a modified commercially available human device for use in dogs and cats when performing stereotactic radiosurgery. The system described is the one that we still use clinically at the hospital.

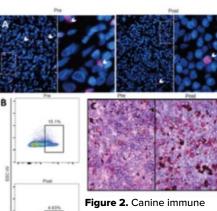
Ongoing Research – Mapping the Mutational Load in Dog Tumors

As a tumor develops it can accumulate many different mutations, which give it its malignant characteristics. In order to better understand how tumors develop and how to better target them, we need to map the changes that occur in genes and proteins.

- We answered an NCI call for collaboration of NCI-Designated Cancer Centers and Veterinary Medical Colleges. We received a grant of \$318,472.
- We brought together a team of 13 investigators across several schools, including the veterinary oncology program and the human cancer center.
- We are looking at glioma, melanoma and osteosarcoma in dogs using whole exome sequencing for analysis of non-synonymous somatic mutational load and RNAseg expression analysis for mutational load and DLA typing. We are also immunophenotyping and analyzing the tumor microenvironment to assess the potential for immunotherapy in these tumors. We are using 30 banked and 5 new tumor samples.

"UC Davis provides a collaborative and creative atmosphere where ideas can thrive and I can pursue my passions."

Dr. Jennifer Willcox



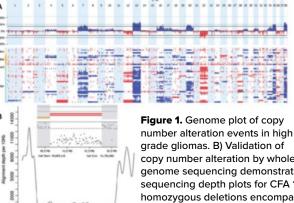


monitoring A) Tumor infiltrating Tregs by IF and flow cytometry (B) demonstrating a decrease after RG + immunotherapy. C) Tumor infiltrating CD8+ cells by IHC demonstrating an increase after RT + immunotherapy.

Initial work showing immunological responses to radiation and immunotherapy. We have developed a recognized expertise in being able to analyze the dog's immune response.

> **Preliminary work** showing mutations in

dog glioma.



copy number alteration by wholegenome sequencing demonstrating sequencing depth plots for CFA 11 homozygous deletions encompassing the INK4A/B locus in a glioblastoma.

UC DAVIS VETERINARY ONCOLOGY • PROGRAM UPDATE 2018 • 35

Research Publications – Creating Impact and Spreading Knowledge

VALIDATION OF AN INDEXED RADIOTHERAPY HEAD POSITIONING DEVICE FOR USE IN DOGS AND CATS

KATHERINES, HANSEN, ALAIN P. THEON, SONIA DEFERICIE, MICHAEL S. KENT

Introduction	(CT) scanner o
As a storage time to the storage of the radiation does with the storage of the s	a flat table, lass (GTV) include tumor-related tumor volume margin to acco The planning tu around the CTV positioning (eg and light-redat of imaging, an movement. ⁴⁴) small contribut the head and no amethesia, into weterinary patie
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Fro Surgery (Hanse diation Fue-Portion Veterin College Add

Area:

Radiotherapy

Impact:

Setup variability affects the appropriate delivery of radiation and informs the setup margin required to treat radiation patients. This paper described the use of a head and neck positioning device that is indexed to the linear accelerator for use in treating dogs. This system is the one we use clinically to treat our patients receiving intensity modulated radiotherapy for tumors in the head and neck.

Journal of Anian Medicine and Surgery 29(4):000-000, 2015

Clinical Report

Chronic T-cell Lymphocytic Leukemia in a Black Swan (Cygnus atratus): Diagnosis, Treatment and Pathology Kristin M. Sinclair, DVM, Dipl ABVP (Avian), Michelle G. Hawkins, VMD, Dipl ABVP (Avian), Lewis Wright, DVM, R. P. Chin, DVM, MPVM, Dipl ACPV, Seau D. Owens, DVM, Dipl ACVP, Dval Sancher-Mighalen Gurman, IV, MS, Dipl ECZM (Avian), DACZM, Michael S. Kent, DVM, Dipl ACVVM, DIPL ACVR, H. L. Shivaprasad BVS, END, DACVP

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Case Report	animal care staff and had an unremarkable medical
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Area:

Leukemia

Impact:

This paper describes diagnosis, treatment and pathology of a black swan from a local zoo with chronic Lymphocytic Leukemia. This is the first report of this disease in this species and documents a treatment course and outcome.

UTCOME OF DOGS WITH INTRANASAL LYMPHOMA TREATED WITH VARIOUS RADIATION AND CHEMOTHERAPY PROTOCOLS: 24 CASES

REBECCA GEORGE, ANNETTE SMITH, STEPHANE SCHLEIS, WILLIAM BRAWNER, GREGORY ALMOND, MICHAEL KENT, JACKER WYRL, JUAN BORREGO, ANTONY MOORE, MICHAEL KEYTELERER, SARAH KRAIZ

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Area:

Lymphoma

Impact:

Canine intranasal lymphoma is an extremely rare disease and studies evaluating the effectiveness of treatments are uncommon. This multiinstitutional study looked at survival time of dogs treated with radiation and/or chemotherapy. Results support the use of radiation therapy, and provide much needed information for the treatment of this disease as well as information for owners on prognosis so they can make informed treatment decisions.

Journal of Veterinary Internal Medicine

fer Juan Med 2016;32:1112 1120 Treatment of MRI-Diagnosed Trigeminal Peripheral Nerve Sheath Tumors by Stereotactic Radiotherapy in Dogs K.S. Hansen, A.L. Zwingenberger, A.P. Théon, I. Pfeiffer, and M.S. Kent

and Surrotatic redictheneys (SRT) is an energing technique for treating tasters in azietals. arrival was 245 days (mage: 99 1323 days, n = 6). No signs of sense adverse effects of or militrics effects versus waves researches could not be conformed histocerthalosies?b

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ucoulle, TN (Pfo)for). All work was performed at the Villans R. Pritchard Veterinary Medical Teaching

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Area:

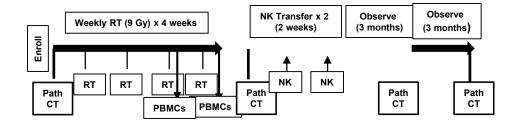
Trigeminal Peripheral Nerve Sheath Tumors

Impact:

This study assessed the outcome of dogs with intracranial trigeminal nerve peripheral nerve sheath tumors that were treated with stereotactic radiotherapy. The study provides preliminary evidence that dogs benefit from this treatment in terms of long term survival and that it is well tolerated and requires fewer anesthetic events than conventional treatments.

Combined RT and Locally Injected Autologous NK Cell Therapy in Dogs with Osteosarcoma

Osteosarcoma, a type of bone tumor, is a disease that affects both children and dogs. Less than 1,000 children a year develop this type of tumor, yet, more than 10,000 dogs are diagnosed with this tumor each year. While we are able to treat the local tumor effectively, the spread of tumor to the lungs kills both children and dogs. In this National Cancer Center-sponsored trial in dogs, we developed a way to collect, grow and activate a dog's own natural killer cells and inject them into the tumor after irradiating it to train these cells to seek out tumors throughout the body. Preliminary results from this trial are promising and show that radiation can enhance natural killer cell cytotoxicity. The paper has just been accepted into the Journal for ImmunoTherapy of Cancer and will soon be published.



Treatment schema for combined RT/NK immunotherapy targeting cancer stem cells and other tumor cells in dogs with locally advanced osteosarcoma.

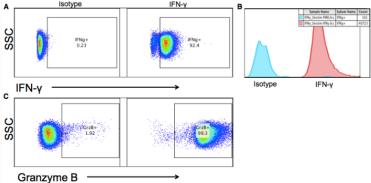
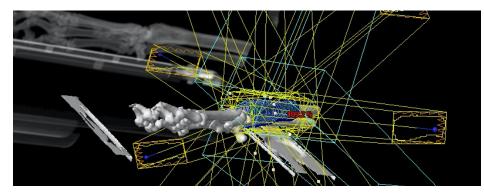


Figure 4. Expanded Canine NK/LAK Cells are Highly Activated. At days 7, 14, and 21, 5 - 10 x 105 cells were recovered from co-culture for phenotyping by flow cytometry. Following 4 - 6 hour stimulation with PMA (20 ng/ml) and ionomycin (1 µg/ml), the expanded cells were stained for intracellular expression of activation/cytotoxicity cytokines Interferon gamma (A) and Granzyme B (C). Histograms of median fluorescence intensity of IFN-y by flow cytometry are shown for NK cells (red) and isotype (blue). Representative panels are shown.



Radiation plan from a dog with an osteosarcoma in his distal radius.

Results of surgical excision and evaluation of factors associated with survival time in dog with lingual neoplasia: 97 cases (1995–2008)

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	Michael S. Kent, 2014, DACOR, DACOR; Philipp D. Mayhew, mass, DACOS; Dorothy C. Brown, DVM, DACOS



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Area:

Lingual Neoplasia

Impact:

This multi-institutional study describes the clinical characteristics, treatments, outcomes, and factors of dogs with lingual (tongue) cancer that were treated with surgery. We found the most common tumors were malignant with squamous cell carcinoma and malignant melanoma predominating. We found that the tumor size at treatment was important in determining outcome supporting early detection and treatment.

	Description Weinemarky Moduline 128 (2016) 126-124	
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1000	Preventive Veterinary Medicine	
ELSEVIER	journal homepage: www.elsesier.com/ocate/precetmed	16 1

LF. Schmidt ^(k) , (¹ / ₂ , ¹ / ₃ , ¹ / ₄ , ¹ / ₄), ¹ / ₄), ¹ / ₄ , ¹ / ₄), ¹ / ₄ , ¹ / ₄	
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1. Introduction	chemotherapy can entend median survival beyond these 5 months (Balley et al., 2000; Chan et al., 2000, 2000; Straw et al., 1991; Val
Surgically treated dogs with appendicular osteosarroma (OS).	er al. 2002).
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have a median survival time of 5 months (brodey and Abr, 1976;	(IFCEAA), we constructed a multivariable prediction tool, predict
Cooley and Waters, 1997; McNeill et al., 2007; Norodin et al., 1989;	ing a dog's risk of montality at 5 months and 1 year after receiving
Paret al., 1998; Spodoick et al., 1992; Straw and Withows, 1996). For	surgical treatment for OS (Schmidt et al., 2013). This tool predicts
the average potient, previous studies have shown that additional	mortality risk based on a patient's age, weight, gender, neuter sta-
	tus, serum alkaline phosphatase (SALP) level, breed, and tumor incation. In a nested study, we explored whether chemotherapy
	incation. In a mented study, we explored whether chemotherapy effectiveness differed between dats with a different predicted that
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Area:

Chemotherapy and Osteosarcoma

Impact:

Canine osteosarcoma is the most common bone cancer and an important cause of mortality in large, purebred dogs. The study confirmed that the existing multivariable risk prediction models can predict a patient's risk and that dogs with a relatively low mortality risk benefit the most from chemotherapy. This can be used to help guide owners in deciding on treatment options.

Boolwell 54 March 2017 | Boolwell 2 May 2017 | Accepted 9 May 2017

ORIGINAL ARTICLE

Patient characteristics, prognostic factors and outcome

of dogs with high-grade primary mediastinal lymphoma

WILEY VILLEY

E. L. Moore¹ | W. Vernau² | R. B. Rebhun³ | K. A. Skorupski³ | J. H. Burton

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Area:

Lymphoma

Impact:

This retrospective study looked at dogs with mediastinal lymphoma to determine outcomes and prognostic factors. The results suggest that survival may be improved with treatment using a CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) based chemotherapy protocol.

Omparative Oncology

Clinical presentation, treatment and outcome in 31 dogs with presumed

primary colorectal lymphoma (2001–2013)[†]

L. Dennas¹ (J. H. Burton³, G. Post², O. Kristal¹, M. Gauthier¹, J. F. Borrego¹, A. Di Bella¹ and A. Laza-Guecia¹ ¹Pand stated Conce one, Experiment of Clinical Science, Odreads free University, For Collin, CO, 188. ¹Dis Versing Concer Center, Nervoki, CT, USA

* Makalangko kuman kenamp hangangko propin da hanam kernas Catasta, Co, Cat Sakada (* Visiting Kalasa), Dohendrig Halanon Weenam, Jakahan, WU, USA * Yon Sim Malmah, Makalan Ferrian, Glagoro, US. Abstract The alignetist of this renditionense retrospective study was to desothe clinical presentati and outcome and to determine programic factors for dogs with presumed primary of and outcome and to determine programic factors for dogs with presumed primary of the distribution.

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Area:

Lymphoma

Impact:

This multicenter study looked at clinical presentation, treatment and outcome of dogs with colorectal lymphoma. It was determined that dogs with colorectal lymphoma have considerably longer progression free survival than other forms of non-Hodgkin's lymphoma. This study provides information for a relatively rare type of lymphoma and shows that it can be treated. One of the oncology program's aims is to develop new drugs and therapeutics. Monoclonal antibodies and immunotherapy are changing how cancer is treated in people. To date, no effective monoclonal antibodies have been developed for dogs. Monoclonal antibodies can be used to target cells that express tumor markers or can be used to enhance immunotherapy.

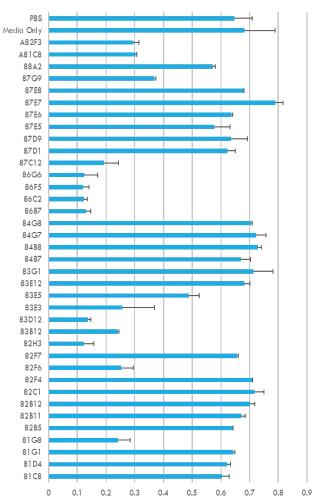
Over the past year, we have been working with researchers at the Center for Comparative Medicine to develop monoclonal antibodies that act as a type of immunotherapy that can be used as a sole treatment or in combination with other therapies.

The first part of the project is complete, having developed multiple antibodies that we are now screening to identify the most effective candidates.

"UC Davis has a long history in comparative oncology. Gordon Theilen, an Emeritus Professor at UC Davis, is one of the founding fathers of veterinary and comparative oncology. This history, combined with the tremendous potential that comes when a leading veterinary school is partnered with an NCI designated Comprehensive Cancer Center, is ultimately what convinced me that I needed to be at UC Davis."

– Dr. Robert Rebhun





Blocking ELISA was used to screen many PD-L1 antibody candidates to assess their effect to block PD-1 / PD-L1 interaction.

PLOS ONE

NEEMOLIMICLE A Comparative Oncology Study of Iniparib Defines Its Pharmacokinetic Profile and Biological Activity in a Naturally-Occurring Canine Cancer Model

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CPEN ACCESS Chefon: Sale C, Pactra M, Macde V, Burton JH, Smith A, et al. (2016) A Crocking Study of Inpath Defres to Pharmacistedic holle and Biologics Naturahy-Councing Carlies Cancer M OME Tricity and Heff A doi:10.1137/1gr

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Abstract

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PLOS ONE | DOI:10.1371(cumal.pone.0149194 February 11, 2

Journal of Veterinary Internal Medicine

Frequency and Severity of Neutropenia Associated with Food and Drug Administration Approved and Compounded Formulations of Lomustine in Dogs with Cancer

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Compounding in the emtorized proparation of drugs that are not commercially available in the interior formulation or strength. Compounding of verments of the lask of available food and in the propagation of the lask of available food and the last of the lask of available food and the last of the lask of available food and the last of the lask of available food and the last of the lask of available food and the last of the last of available food and the last of the last of the last of the last in the last of the last in the last of the last of the last of the last in the last of the las

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Area:

Comparative Oncology and Iniparib

Impact:

This multicenter study run through the NCI assessed pharmacokinetic exposures and tolerability of iniparib, a new chemotherapy agent being developed for humans. While it was shown this drug could be given safely as a single agent and in combination with carboplatin over a range of doses, clinically relevant concentrations of the parent drug and selected metabolites were not detectable in canine tumor tissues at any studied dose, thus eliminating expectations for clinical responses in dogs or humans. While it was a negative study, it did inform the NCI that this drug was not likely to work in humans either and stopped it from going into trials in people where it would have failed.

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Rod L. Balhorn*, Katherin Teri Guerrero ^b , Robert B.	e A. Skorupski ^b , Sapl Rebbug ^{b,*}	hon Hok ^c , Monique Cosman Balhorn ⁴ ,
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Arkide bisney; Becineti 29 March 2010 Becineti in reched from 19 May 2010 Angreent 29 May 2010 Expression Expression RA Back Dave 1	A STRACT There are suggested and the second sector of surface protons have suggested and sector of human patterns with non industrial pathwares, 20(11) is speaded that undust immuno- terns of the second sector of the second sector of the second sector of the human and cause explores than human the second sector of such the second sec- tor and the second sector of the second sector of the second sector of human sector of the second sector of the second sector of the second human sector of the second sector of the second sector of the second human sector of the second sector of the sector of the sector of the human sector of the sector of the sector of the sector of the sector of the human sector of the sector of the human sector of the se	
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1. Introduction Human B-cell lymphocytes e surface proteins that continue to often over-responsed (an much face-ofmazignancies-derived foron (Belamanet al., 1991; Schwarman (Polisium et al., 2007), CD2/Hu/(Bozzi- (2)), CD2/Hu/(Bozzi-	o be produced, and are at 10-fold), on the sur- theselymphocytes. (D19 nand Racila, 1995). (D20 kins et al., 2003). (D37	Ecomplexpension H&A DR (Dproint et al., 1987) fines et al., 1960) are only a few examples of the receptors that have been as the second second second second second second or therapeutic argening of lynaphenes. The retention of herad second are of statice proteins on various forms of 8-cdl hypotheses and bekensis has led to the development of a satisfy of antidexp land limitory for tracing harman room Hodglion's hypothese (2011) and for tracing harman room Hodglion's hypothese (2011) and for tracing harman room Hodglion's hypothese (2011) and other B = cdl hypotheses. Arthologies to C2019 have been as the second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second second
		coupled to toxins and have shown efficacy in treating acute lymphocytic leukernia and Nill, both in vitre and in

Area:

Lymphoma

Impact:

Cure rates for people with lymphoma are better than that of dogs and cats. We need to improve our understanding of pet cancers at the molecular level to allow development of more 'targeted' therapies for cancer in pets. This work demonstrated that canine and human B-cell lymphoma expressed similar levels of a molecule that could be targeted with a small-high affinity ligand. Additional work is ongoing to determine the effects of chemotherapy on expression of this molecule. Further collaborations with the Center for Comparative Medicine are now underway to develop canine specific antibodies that target canine tumors and/or activate the immune system to target cancer.

Area:

ACVIM

Efficacy of Compounded Cancer Drugs (Lomustine)

Impact:

Compounding of veterinary drugs is performed because of lack of available Food and Drug Administration approved drugs for animals. However, sometimes compounded drugs are not as effective. It was determined that dogs given compounded formulations of Lomustine experienced fewer neutropenic events compared with dogs given FDA approved formulations of Lomustine.

ember 2016 Accepted: 1 December 2016

KEYWORDS canine, chemotherapy, feline, oncology, veterinary

1 INTRODUCTION	compounded product. ⁶ In addition, potency of the compounded formu- lations for 5 different compounding pharmacies ranged from 50% to
Overnotherapy drugs are commonly compounded in veterinary medi-	115% of the labelled concentration with only 1 of the samples within
cine to ensure smaller pets are safely dosed, to provide drugs in for-	50% of labelled concentration, which is the requirement for FDA
mulations that clients are able to administer to their pet, or when	approved formulations. Evaluation of potential differences between
Food and Drug Administration (FDA) approved formulations are una-	compounded and FDA-approved formulations of lomustine was
vallable. However, there is growing concern as to whether com-	initiated as there was a clinical suspicion that neutropenia, and possibly
pounded medications are similar in efficacy to and of similar quality	tumour response, was occurring less frequently when dogs were trea-
as FDA-approved products. Previous studies have evaluated omepra-	ted with compounded lonustine. Potential differences in potency
zole for horses and itraconazole, trilostane and ciclosporin in dogs	between compounded and FDA-approved product may not be as read
and found that these compounded products were not equivalent in	By detected clinically with chemotherapy agents that are generally well
potency and resulted in treatment failures more frequently than the	tolerated by most dogs and cats, such as chlorambucil, melphalan and
FDA-approved versions of the drugs. ³⁻⁴	metronomic (low-dose) cyclophosphamide. In addition, these drugs and
Recently, our group demonstrated neutropenia that occurred with	frequently used to treat more slowly progressing cancers and tend to
greater frequency and severity in dogs treated with FDA-approved for-	be administered for a number of weeks before response to treatment
mulations of lomustine as compared with dogs administered a	can be assessed.6-9 Side effects associated with chlorambuch

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Area:

Efficacy of Compounded Cancer Drugs (Chlorambucil, Melphalan and Cyclophosphamide)

Impact:

Oral chemotherapy is frequently compounded in veterinary medicine, however, the potency of some formulations have been shown to vary from that of the FDA approved products. This is important because if too much drug is in a given capsule it can result in toxicity while if too little is present it will be ineffective. The results of the study demonstrated the variability of compounded medications and highlighted the need to consider this when prescribing these medications. It also highlights the need for more oversite of compounding pharmacies to ensure patient safety.

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Area:

Transitional Cell Carcinoma

Impact:

This study looked at efficacy of piroxicam in combination with either mitoxantrone or carboplatin in treating transitional cell carcinoma. The study did not detect a difference in outcomes between dogs treated with either mitoxantrone or carboplatin in combination with piroxicam indicating both are effective first line therapies.

e Oncology ginal Article

Treatment of feline intermediateto high-grade lymphoma with a modified university of Wisconsin–Madison protocol: 119 cases (2004–2012)

 A. Golden¹², S. D. Allhad¹⁴, E. M. Chou³, W. Yomu², A. N. Smith, J. C. Garerty, K. C. Oro, B. K. B. Chou³, C. O. Rochiguez, P. J. and J. C. Barrot, K. C. Oro, B. K. B. Chou, S. S. C. S. Rochiguez, P. J. and P. Sterner, M. Start, S. S. Sterner, Y. G. Karne, Parc, In K. S. W. Young Stress, Using Strength Theory of Collins, Parc, Inc. O. X. W. "Operating stress, Using Strength Theory, and Start, S. W. "Operating of Proc. Stress, Phys. Rev. B 10, 1000 (1997). "Operating of Collins, Phys. Rev. B 10, 1000 (1997). "Operating of Collins, Phys. Rev. B 10, 1000 (1997). "Operating of Collins, Phys. Rev. B 10, 1000 (1997). Coll. Coll. "Operating of Collins, Phys. Rev. B 10, 1000 (1997). Coll. Coll. Coll. "Operating of Collins, Phys. Rev. B 10, 1000 (1997). Coll. Coll. Coll. Coll. "Operating of Collins, Phys. Rev. B 10, 1000 (1997). Coll. Col

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Area: Lymphoma Treatment in Cats

Impact:

There was limited information regarding CHOP based therapy, a multidrug chemotherapy treatment, for cats with lymphoma even though it is widely used in treating this disease in this species. This study determined that CHOP therapy significantly lengthened survival time and is a viable first line treatment.

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Journal of Veterinary Internal Medicine

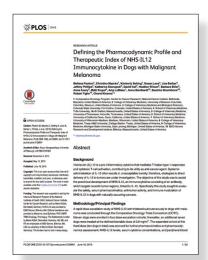


Area:

Transitional Cell Carcinoma and Bacterial Urinary Tract Infections

Impact:

This study examined incidence and contributing factors to urinary tract infections in dogs with transitional cell carcinoma. The study found that it is important to regularly monitor for bacterial infections of the bladder in dogs with this disease. In addition, tumor location and sex may be predictive and can help clinicians asses risk accurately.



Area:

Melanoma

Impact:

In this NCI organized multicenter trial the efficacy of a new formulation of interleukin 12 was tested in treating dogs with lymphoma with the goal of helping to understand how to use this drug in people. This study successfully defined a narrow therapeutic window for systemic delivery of NHS-IL12 via the subcutaneous route. Results will inform the design and implementation of first-in-human clinical trials of NHS-IL12 in cancer patients.

Journal of Veterinary Internal Medicine

Standard Article

Evaluation of Weight Change During Carboplatin Therapy in Dogs With Appendicular Osteosarcoma A.L. Story O, S.E. Boston, J.J. Kilkenny, A. Singh, J.P. Woods, W.T.N. Culp, K.A. Skorupski, and X. Lu

Buckground: The province of uncer exclusis in ventrinary multite has not been multial widely, and as if yet, so distributed approach extrate about the production is ventrinary patients. The production of the And change is a signific preparation investor on extension of a strength of the second stre t increase in weight occurred over the course of chemotherapy, but this change was not statistically signifi-g did not have a significant effect on survival. Institution, patient sex, and serum ALP artivity did not ner Weight change was not a prognostic factor in these dops, and weight loss alone may bina cancer cacheria in doas with arecenfactor extremeroma.

thed in poster form at the Feterinary Orlands, Florida, October 2016, 1. Store, DOI 1027 Nob. for for 407

INDIRECT COMPUTED TOMOGRAPHIC LYMPHOGRAPHY FOR ILIOSACRAL LYMPHATIC MAPPING IN A COHORT OF DOGS WITH ANAL

SAC GLAND ADENOCARCINOMA: TECHNIQUE DESCRIPTION

STEPHANE A. MARINE, MICHELE A. STEPTEY, MARK FULLER, GERALDONE B. HUNT, PRILIPP D. MAYREW, RACHEL E. POLLARD

er in dogs with anal sac gland carcinona, providing a pe uph node identification in dogs. Thirteen adult dogs di in this prospective, pilot study, and ICTL was perform

d lymphatic pathways and sentin ipsilateral to the anal sac gland -

ies have shown that dogs are

b) boy communication to a vehicitary encodeg In that study, 45% of the degs had caches as a BCS 35 of 9 and 15% percent had me severe manche wasting.⁴ The investigators that BCS alone may not be semitive encode cancer cachesia. A similar study of 57 cars 2016. Reviser reviews based when Annual of Venerary based risk and survival time in human cancer patients.^{1/2} retrospective study assessing weight change duri

Area:

Osteosarcoma

Impact:

Cancer cachexia, a syndrome of inflammation. loss of

muscle mass and weight loss in the face of cancer is not well studied in veterinary medicine. In this 3 institution study dogs with osteosarcoma treated with surgery and chemotherapy were evaluated for weight loss over the treatment period. Dogs in fact gained a small amount of weight over treatment and further, weight change was not a prognostic factor in dogs for survival. Weight loss alone may not be a suitable method of determining cancer cachexia.

Ultrasound and computed tomography of the iliosacral lymphatic centre in dogs with anal sac gland carcinoma

R. E. Pollard¹, M. C. Fuller² and M. A. Steffey¹ ¹Department of Suggial and numericone control of California, Davis, CA, USA Davis, CA, USA ¹⁰⁰ and ¹⁰⁰ Andreat Teaching Hospital, University of California, Davis, CA, USA

	Introduction	doubles to the left and/or right of midline. ¹ Th medial iliac LNs receive afferent lymphatic vessel
	Anal sac gland carcinorma (ASGC) is the most common malignancy affecting the anal sacs, and accounts for 17% of perianal tumours in desgs ^{1,1} ASGC tends to be a locally aggressive non- plans, which often metastasians to regional proph- nodes (LNM) early in the course of disease ^{1,2} . Distant metastatic lesion more commonly develop hate in the disease encoces, with the liver, selece	from the internal iliac and sacral LNs and togethe comprise the iliosacral lymphatic centre. The inter- nal iliac LNs (also referred to as hypogastric LNs reside in the ragion vertraft to the sixth and severe lumbar vertibres and can be located as caadal the lumboscent space. The variably present medii and lateral sacral LNs lie vertraft to the sacratus as
Invespendence address En Poland, DMA, PHD Ispartment of Surgical and Radiological Sciences dood of Winestawy tecklone Surgical Coldonias Inels CO (5558), DSA esait guellard puolarise du	tate in the detect process, with the inter, piece and hange being the next common busices. ¹⁴ Motarticlication have been identified after time of agnories in C ⁻² years, with the methal like USs being the model accounts on the identification to medial like. Use any regulty particular to the left and like of mality, works in the first of suth handre redutes and between the deep circumfic- lies and external line arthress in a comissional field and the arthress line arthress in a comissional field and. ²	canali vertificae ¹ Therapy for ASCC is directed towends both the primary lesion and materiatic disease. If present disease of the primary lission, presence or observed materiatic disease and modelity of therapy, with range from 292 to 950 days ²² . Anal succeletors with excision of materiatic XDs is a currently the transmitter of observed. ² Adjuance disease is other presented for patients with evidence of materiatic disease. ^{2-5,10}

Area:

Lymph Node Identification

Impact:

Both ultrasound and CT can be used to identify lymph nodes in a patient undergoing staging for cancer. This study is the first to directly compare these two modalities in looking for lymph nodes. Contrast CT was able to identify more lymph nodes overall, although ultrasound was superior in some cases in finding abnormal lymph nodes. This suggests that overall both imaging modalities have their use.

Area:

Anal Gland Adenocarcinoma & Sentinel Lymph Node Mapping

Impact:

Sentinel lymph node mapping can help disease detection and surgical planning in patients with complex lymphatic pathways, determining the lymph node most likely to be affected by cancer. Results from this study show that using a contrast agent and a CT scanner you can identify which lymph nodes should be removed to check for disease and to therapeutically treat patients.

Reariest: 6 January 2016 Accepted: 8 Neversiter 2016 DOI: 10.1111/star.10174

ORIGINAL ARTICLE

Mechanical properties of canine osteosarcoma-affected antebrachia*

Michele A. Steffey¹ | Tanya C. Garcia² | Leticia Daniel¹ | Allison L. Zwingenberger¹ | Susan M. Stover²

Department of Surgical and adiological Sciences, School of	Abstract
rterinary Modicine, University of diformin Davin, Davin, California	Objective: To determine the inflaence of neoplasia on the bioenchanical propert of canine antebrachia.
Department of Anatomy, Physiology	Study design: Ex vivo biomechanical study.
d Cell Biology, School of tterinary Modicine, University of diformin Davis, Davis, California	Sample population: Outosarccena (OSA)-affected canine antebrachia (n = 12) a unaffected canine antebrachia (n = 9).
errespondence ichele A. Steffey, Department of ogical and Radiological Sciences, hocl of Veterinary Medicine, siversity of California Davis, 1	Methods: Anthrachis were compressed in axial loading until failure. A to deformation caree was used to acquire the structural mechanical properties of m plataic and analitectal specimens. Structural properties and properties somainted body weight (EW) and radius length were compared using: analysis of variar (ANDVA)A. Modes of failure were compared descriptively.
inlda Ava, Davis, CA 99616. malt: maint/fry@walkvis.edu anding Information aivenity of California.Davis noter for Companion Animal odds	Renaits: Nonplatic antentiatis futured a, or Algore to, the OSA in the do- radial displays: Audited an attending lifest via mid-displays and radial discu- with a transverse carial component and an obligar cashal component. Structures mechanical properties were more variable in sequelatar attendients than auffect antenduals, which was parality attendarabe in differences in home genomey rela- tion days and the second of by day that radial based to the second on days day. When accordingly attendarabe in differences in home genomey rela- nsengy to yield and failure, were lower in neoplatic antenderis than is muffec- antendarab.
	Conclusions GNA of the datal and an acquispla in dapa presented for line war lation markedpy components where investmal singuppy of affordal antehexic However, homechanical properties of affordat bone was sufficient for weight bearing, as more of the anophatic antehexicals farctured before anoptation. The behavior of name invaded bone under cyclic loading warants (infertur investigation to evaluant the visibility of in six the mapping for bone menors in daps.

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Area:

Osteosarcoma

Impact:

In this study limbs from dogs were collected after amputation and the structural integrity of these bones affected by bone tumor was studied in the lab. We found that these cases were capable of bearing weight but would fracture at a much lower load than normal bone.

Outcome following treatment of feline gastrointestinal mast cell tumours L.E. Barrett¹ | K. Skorupski² | D.C. Brown¹ | N. Weinstein³ | C. Clifford⁴ | A. Szivek⁵ | Haney⁴ | S. Kralza⁶ | E. L. Kric

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Rectired: 13 Anuary 2017 Revised: 16 April 2017 Accepted: 3 Ho

ORIGINAL ARTICLE

Area:

Feline Gastrointestinal Mast Cell Tumors

Impact:

The prognosis for cats with gastrointestinal mast cell tumors is poor and has limited treatment options. However, this study determined that the prognosis may be better than previously thought. Surgical and medical treatments were associated with increased survival times. Also, cats may benefit from more aggressive treatment than prednisone, a steroid, alone which is commonly used to treat this disease.

Marphy et al. BMC Viteriney Research (2017) 13:18 DOI:10.1186/012913451113-5 BMC Veterinary Research Evaluation of P16 expression in canine

appendicular osteosarcoma B. G. Munthy¹⁷, M.Y. Mok¹, D. York², R. Rebbur², K.D. Wookerd¹, C.

Area:

Canine Appendicular Osteosarcoma

Impact:

P16 expression by canine OSA tissue is predictive of clinical outcomes. The identification of a molecular marker for canine OSA is an important goal and the results justify a larger study.

Area: Lymphoma

Impact:

This study was done to determine the characteristics of dogs with mediastinal lymphoma and to determine outcomes as little was known about this disease. The results suggest that survival may be improved with treatment using a CHOP based protocol.

PAPER

Association between environmental factors including second-hand smoke and primary lung cancer in dogs

ZERENBERG-RIPOLE*, R. E. POLLARD', S. L. STEWARF, S. D. ALLSTRET, L. E. BARR

os: In this case-control study, an owner survey was ristics, general health care and e omas formed the Case group. Dogs diagnosed with mast cell tu oup 1 and dogs diagnosed with lung tumour and nations and e

mum: A total of 1178 owner summs were mailed and 470 a B Games surveys were used in Control Group 1 and 166 dogs

ound in dogs. The results of this study may not be



Area: Second Hand Smoke and Lung Cancer in Dogs

Impact: This study was conducted as a survey to see if dog lung tumors were associated with exposure to second hand smoke. An association with exposure to second hand smoke and prevalence of lung cancer was not identified in dogs. However, study limitations may have precluded detection of an association.

Dalis, California Dalis, California, Normingto, S. Sanashnare ef Reingland Sharingson, Sanashna Januarykar, Gattania, Danis, Dalis, Sanashna Taquahaman, H. Sanashna, Dalis, Sanashna California Sanashna ef Gattania, Davis, Danis, California J. H. Bertin, Danishna, H. Gattania, Dalis, Sanashna, S. Sanashna, S. Sanashna, Davis, J. Shash, Januar, J. Sanashna, Davis, J. Shash, Januar, Davis, G. Sharish, Davis, J. Shash, Januar, Davis, G. Sanash, Davis, J. Shash, Januar, Davis, J. Sanashna, K. Sharish, January, Sanashna, Davis, Sharish, Sanashna, Sharish, Sanashna, Sanashna, K. Sharish, January, Sanashna, Sanashna, K. Sharish, January, Sanashna, Sanashna, Sanashna, Sharish, Sanashna, Sanashna, Sanashna, Sharish, Sanashna, Sanashna, Sanashna, Sharish, Sanashna, Sanashna, Sanashna, Sharish, Sanashna, Sanashna, Sharish, Sanashna, Sanashna, Sharishna, Sanashna, Sanashna, Sanashna, Sanashna, Sanashna, Sharishna, Sanashna, Sanash	From A and of 2 days are standing in which is sensitive to some at the labor source of the labor source o	
1 INTRODUCTION Significants loss of the rank convents and and is entravated ascents for 361 a 264 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 264 and 2	of all carine turnours and on. ¹ The majority of diggs mathematic disease, and disease sutting has been editation involvement is which lymphorsa, and for i involvement is reported if the presence of a mul- net. T-cel plenetype, and with a warve outcome as	In the momentum numerical the approximately, SA of ours, Sange appeared properties of the same set of a colorability of the outper set of the old sign of a colorability of the same set of the old sign of a colorability of the same set of a colorability and the same set of the same set of the same set of the same model. (JACOP E. Capacipano, molecular same set of the same model, and and a same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same set of the same se
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Patient characteristics prognostic factors and outcome

of dogs with high-grade primary mediastinal lymphoma

mau² | R. B. Rebhun³ | K. A. Skorupski³ | J. H. Burton³

motive survey Pe, partir regions; BBC, is VMIRA Velocity Medical Tracking Back therapy and medicatinal insolution.^{10,10} To the authors' knowledge therapy and medicatinal insolution.^{10,10} To the authors' knowledge No. Come Carlot 1987.1

Rectinet 14 March 2217 Review 2 May 2517 Acces

ORIGINAL ARTICLE

Original Article

CHOP chemotherapy for the treatment of canine multicentric T-cell lymphoma

R. B. Rebhun¹, M. S. Kent¹, S. A. E. B. Borrofka¹⁺, S. Frazier¹, K. Skorupski¹

Centerpondence of It.D. Anthum Department of Sur Rociclogical Scen and The Compared Case Grant 2112 Tabler Hall Case Scienti Avenue University of Cable David, CA (Ballio USA email Case Scienti Avenue USA

	Introduction	(stage (II-V) disease, inclusion of canics patients
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Labi	*Current address: University Claicine Companies Ariendo, Division of Diagnostic Reaging, Yaldonatella, 5564 CM Unavide The Netherlands.	for fint-line therapy of dogs with multicentric (stages (11-V) T-od NHL that were resultable

riginal Article

Identification of occult micrometastases and isolated tumour cells within regional lymph nodes of previously diagnosed non-metastatic (stage 0) canine carcinomas

K. M. Casey¹, M. A. Steffey² and V. K. Affolter

	Introduction	in which injection of vital dye, most common
Correspondence address: K. Gory Department of Portodogo, Microbiology and Immandogy Williers R. Probadi Watering Heddel Machina J. Buelde Williers R. Probadi Watering and California. Davis USA: Diselections. Davis USA: Coloris USA: e-mail Immandel Machineski Immandel Machineski Microscopy functionicedu	Table distribution of tamour minutums within regional hypothesis in a searatic accorporate of ranging, and thus pregnostrations, of both cames and human automaticas. Ratify identification of types- platic mataneous hards the potentially impact particu- tations for million the analysis within a line standard strategies of the standard strategies and the strategies and the strategies and the strategies and annuous basistic hardweight inpriving annuming times addite response to adjusticity fempriss. Accurate Mathematicas of the correct hypoth odditis to sample has list to the development of stratinal hypoth out CEUS mapping tradinators.	coupled with regional and intersectionity in priore improvements and the identifications of first hyperhouse in a chain documented to due that transmiss buch internisis human cancers, specially the structure of the structure buch due to the structure buck due to the structure

Area:

Lymphoma and Chemotherapy

Impact:

Many historical studies have not accounted for the subtype of lymphoma when evaluating response to treatment. Lore has it that T-cell lymphoma dogs do not do well with chemotherapy leading many to not recommend treatment for this disease. This was the first study to specifically examine the 'gold-standard' treatment for T-cell lymphoma in dogs. This study established a response rate and median response duration in dogs with T-cell lymphoma treated with a standard chemotherapy protocol and showed that this can be an effective treatment. It is critical that such studies are done to establish accurate prognoses for owners to consider when making difficult decisions regarding treatment options for their pets. Such studies are also necessary to establish current best practices when comparing novel therapies being evaluated in current clinical trials.

Area:

Lymph Node Metastasis

Impact:

Identifying even small amounts of disease is important when treating cancer. This study used a specific pathological technique of step sectioning and special stains to evaluate lymph nodes which by conventional methods were thought not to contain cancer cells. In 5 of the 20 cases cancer cells were found indicating this is a better method to check lymph nodes for tumors.

Resolut: 6 July 2006 Revied: 10 November 2006 Accepted: 6 December 2006 ORIGINAL ARTICLI

CT-derived indices of canine osteosarcoma-affected antebrachia strength®

Tanya C. Garcia, MS1 | Michele A. Steffey, DVM, Diplomate ACVS-SA2 O Allison L. Zwingenberger, DVM, Diplomate ACVR² 0 | Leticia Daniel, MV² intern M Stearer DVM PhD Diolomate ACVS

¹ Department of Austones, Physiology and Cell Biology Surgical, Scheek of Victoriany Medickee, Chilomethy of California-Devis, Davis, California ¹ Department of Radiological Sciences, School of Vicentary Medicine, University of California-Devis, Davis, California	Abstract Objective: To improve the prediction of factures in dags with hone tankes of the distal radius by identifying computed ionagraphy (CT) indices that constite with anterchical bone strangth and fracture location. Study designs: Prospective expectational study.
Correputation Models A Deep Department Models A Deep Department Models A Deep Department Department Networks (Section 2014) Notations - Beneficial Department Paralling Biotenation Courts of Comparison Annual Medicine, Eliversity of Collifornia –-Devis	Adduct for per the method is anomatory in p-10, and small calcer two relations of the performance of the pe
1 INTRODUCTION	but the presence of other concurrent orthopolic or neurolog fits the appendicular sket-

orm as: December ; 5(6): 676-684, doi:10.210373ac.2016.08.30.

Modulation of the p53 family network by RNA-binding protein

HHS Public Access

Chris Lucchesi, Jin Zhang, and Xinbin Chen

Area:

Osteosarcoma

Impact:

In this study bones from dogs undergoing amputation for osteosarcoma were studied. The bones underwent a CT scan and then biomechanical testing to see if the CT scan could estimate the strength of the bone and found that it could. This can be clinically used to help predict the risk of pathological fracture in dogs with osteosarcoma if owners do not want to pursue amputation and gives a better understanding of the effects of this disease on bone.

Area:

Modulation of the p53 Family Network

Impact:

Since its discovery more than three decades ago, tumor suppressor p53 has been shown to play pivotal roles in both maintaining genomic integrity and tumor suppression. p53 functions as a transcription factor responding to a multitude of cellular stressors, regulating the transcription of many genes involved in cell-cycle arrest, senescence, autophagy, and apoptosis. However, evolving work is now uncovering that p53, and other p53 family members, are post-transciptionally regulated by multiple NA-binding proteins. Understanding the regulation of p53 by RBPs may open up the possibility for therapeutic interventions.



cible factor 1 alpha is regulated by RB in and a p53 family target, via mRNA

Area:

Tumor Suppressor Gene Regulation

Impact:

Ferredoxin reductase is an important downstream target of p53 that helps regulate killing of damaged cells by a process called apoptosis. This study helped unlock the mechanisms of this protein and the role it plays normally and when its function is lost. We found that Ferredoxin and p53 are mutually regulated and that it is vital in tumor suppression.

Mice deficient in poly(C)-binding protein 4 are susceptible to spontaneous tumors through increased expression of ZFP871 that targets p53 for degradation

iensheng Yan,¹ Aziane Scoumanne,¹ Yong-Sam Jung, Enshun Xu, Jin Zhang, Yanhong Zhang, ang Ren, Pei Sun, and Xinhin Chen.

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Area:

Tumor Suppressor Gene Regulation

Impact:

Poly(C)-binding protein 4 is a protein that is a target of p53 and has been shown to help suppress lung tumors. In this study, we found that mice who are deficient in poly(C)-binding protein 4 have decreased levels of p53 and are likely to develop multiple types of tumors, not only lung tumors. This study found another mechanism of regulating the very important gene p53.

Area:

Regulation of Hypoxia

Impact:

Hypoxia-inducible factor 1 alpha is necessary for cell growth and survival under hypoxic conditions found in tumors. Here, we showed that RNAbinding protein RBM38, a target of the p53 family, regulates HIF1a expression via mRNA translation. Loss of this protein increases RBM38 levels which in turn allow more HIF1a to be made. This is an important mechanism of cancer cell survival in low oxygen environments.



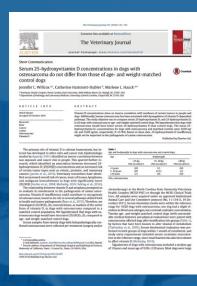


Area:

Rectal Masses in Dogs

Impact:

Colonoscopy in dogs to help diagnose rectal masses is being used more frequently to help plan treatments. This study found that multiple rectal masses in dogs are uncommon, and that colonoscopy was associated with few complications. We further found that with rectal masses it was uncommon to find additional masses deeper in the patient and full colonscopy may not be needed.



TAp63γ and ΔNp63γ are regulated by RBM38 via mRNA stability

and have an opposing function in growth suppres eng Yan', Yanhong Zhang' and Xinbin Chen'

amat spotentiscuto

Area:

Osteosarcoma

Impact:

Vitamin D metabolism can be altered in patients with cancer and in osteosarcoma in particular. In this study blood levels of dogs with osteosarcoma were checked for vitamin D. We found that levels were similar to control dogs and that 25-hydroxyvitamin D insufficiency might not be important in the pathogenesis of canine osteosarcoma.

Interventional Oncology Com William T.N. Culp, van

Dr W.T.N. Culp has served as a labor mall Anim 46 (2016) 553-565

Area:

Interventional Oncology

Impact:

Interventional Oncology is a fourth major cancer treatment category along with surgery, chemotherapy and radiation therapy. Interventional oncology uses targeted minimally invasive procedures performed under image guidance. This review paper introduces this concept to a larger audience to inform them of this emerging area of medicine.

Area:

Tumor Suppressor and Oncogenes

Impact:

P63 is a gene that is related to P53 and thought to be important in cancer. The P63 gene encodes two proteins, DeltaNp63gamma and Tap63gamma. The function of these proteins is not completely understood. In this study we have increased our understanding of these two important proteins and how they are regulated. We found that which protein is made is regulated by the molecule RBM38 and that while DeltaNp63gamma promotes cell growth Tap63gamma acts as a tumor suppressor. Better understanding the mechanisms of cancer allows us to design targets for treatment.

Splenic liposarcoma in dogs: 13 cases (2002–2012)

ta L. A. Gower, over, Julius M. Liptak, swe, sweechesser, William T. N. Culp, over



Area:

Splenic Liposarcoma

Impact:

Splenic Liposarcoma is a rare tumor of the spleen in dogs with little known about treatment outcomes and prognosis. This multicenter case series collected information on this tumor to be able to provide more knowledge for owners and clinicians. We found that dogs without metastasis at the time of diagnosis could do quite well with surgery.

Received 12 January 2017 Accepted 22 June 20 DOI: 10.1111/vm.12738

ORIGINAL ARTICLE

Phrenicoabdominal venotomy for tumor thrombectomy in dogs with adrenal neoplasia and suspected vena caval invasion

Philipp D. Mayhew BVM	&S, DACVS William T. N. Culp VMD, DACVS	
Ingrid M. Balsa DVM	Allison L. Zwingenberger DVM, MAS, DACVR, DECVDI	0

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1 INTRODUCTION Adrenalectory has trafficionally bee more challenging procedures in casi dogs, most adment masses are either	ne surgical oncology. In data suggest that pheochromocytomas demonstrate vascular

ia suggest that pheochromocytomas demonstrate vascular rasion in 33%-55% ²⁻⁵ of cases whereas adrenocortical more invade the vasculature in 2%-22% of cases. ³⁻⁶
note mixed the value that at $z=z_{\rm ex}$ or cases

CC 10.1113/vm.12075

ORIGINAL ARTICLE

Outcome of laparoscopic adrenalectomy for resection of unilateral noninvasive adrenocortical tumors in 11 cats

Jeffrey W. Mitchell, DVM¹ | Philipp D. Mayhew, BVM&S, DACVS¹ | William T. N. Culp, VMD, DACVS² | J. Rend Case, DVM, MS, DACVS² | Ameet Singh, DVM, DACVS² | Mark C. Fuller, DVM, DACVS-SA¹ | Ann Della Maggiere, DVM, DACVS² | J.

¹ Department of Surgical and Radiological Sciences, School of Vatariaary Medicine,	Abstract
University of California-Davis, Davis, California	Objective: To describe the technique and outcomes of laparoscopic advanalectomy (LA) in cuts with advanceostical neordala.
² Department of Small Animal Clinical Sciences, University of Plorida,	Study design: Retrospective case series.
Gaiazeville, Plotida	Animals: Eleven client-owned cats with unilateral adrenal tumors.
¹ Department of Clinical Scalins, Ontorio Ventuary Collaps, University of Oadph, Gardph, Ontorio, Canada "Department of Modifier and Epideminitry, School of Vensinary Modeine, University of California-Davis, Davis, California	Methode: Medical receive of can that underware LA for autiliteral functional adv- al transm at 3 ventransmy anching hangethat were reviewed. Data collectual included algorithment, chinical signs, physical examination findings, diagnostic imaging remash, resperentive holostarity tests, happroceeping of phermater and techniques, Autorian of anothesis and surgary, complications, concentrate procedures, need for comersion to a conse ecitomy, historeab/ordered diamonisk, and sourcentry's narvival.
Correspondence Philipp D. Moylaws, Department of Surgical and Pathidupical Sciences, Sciool of Vorsimary Mathematica University of Calimnia Devis, One Scields Rund, Davis, CA 95955. Finall, philosylaw/Egnall.com	Semiler Herrer ans were helded, 5 with right-field and 6 with the distributions were advected to the preparameters are preparameters are transmort were advected to the preparameters are preparameters are preparated by the transmort and the semi-seminary areas accordingly performed in a still ratio of ≈ 23 , does advected or the same to the cased wave or what hashing to might-dispersion in a seque ordinary, and we per visual index (in ≈ 23 , does advected or the same to the cased wave or the 11 cm were discharged from the loopila, white a median survival from or 100 Jays (mage 40%). T23 Jays) One or all of low meyors processing and cased one of 000 Jays (mage 40%).
	Conclusion: Advanlectomy can be performed in cats via laparoscopy but is techni- cally challenging, and associated with a relatively high conversion rate (36%).
1 INTRODUCTION	of adrenocortical tursors are adenocarcinomas and ar

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Area:

Adrenal Tumors

Impact:

Adrenal tumors can be particularly challenging to remove when they form clots extending into caudal vena cava which is the main vein that runs through the abdomen. This paper describes a technique to remove the clots through the phrenicoabdominal vein which is much less invasive than going into the vena cava.

Laparoscopic Adrenalectomy for Removal of Unilateral Noninvasive Pheochromocytomas in 10 Dogs

Kathryn A. Pitt^{*}, Philipp D. Maryhew², Michele A. Staffey¹, William T. N. Culp¹, Mark C. Fuller¹, Ann Daila Maggiore², and Richard W. Nelsan² ¹Openment of Supplar ArcBadgeon Sterons and Department of Medice and Epidemistry. School of Viterinay Medices, Lin School and Christian School and State School and School a

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Area:

Pheochromocytomas

Impact:

Removing an adrenal gland from a dog can be a difficult and dangerous surgery. Coming up with newer less invasive and safer techniques is vital. This paper described a new laparoscopic procedure for adrenalectomy for adrenal tumors.

Area:

Adrenocortical Tumors

Impact:

More minimally invasive surgical procedures are changing how surgery is done and improving outcomes and recovery for our patients. This paper describes the techniques and challenges for performing laproscopic adrenalectomy in cats.

Principles and Applications ()) of Surgical Oncology in Exotic Animals

Michele A. Steffey, DMA DACVISA

Cancer
 Oncology
 Surgery
 Surgical oncology
 Interventional oncology
 Veterinary

TRODUCTION

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Area:

Surgical Oncology in Exotics

Impact:

This paper reviewed the techniques and approaches required when surgically treating exotic animal species with cancer. Exotic animal species, while less common than dogs and cats are becoming more popular as pets. Further, there are special considerations that need to be taken into account when planning surgery in these animals. Optimal outcomes in surgical removal of cancer are attained by using a holistic approach that includes knowledge of the biologic behavior of the tumor and appropriate staging.

Ninjurin 1 has two opposing functions in tumorigenesis in a p53-dependent manner Batter two in the two in the two in the two interventions in the tumorigenesis of the two interventions and the two interventions in the

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Area:

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Tumor Suppressor Gene Regulation

Impact:

P53 is one of the most important genes in stopping tumor formation and is mutated in the majority of dog and human cancers. Ninjurin is a molecule that is a target of P53 which can in turn modulate p53. We found that Ninjurin can actually enhance tumor growth in those tumors with a mutated P53 while it suppresses them in cells with a normally acting p54 protein. This research is helping to unlock the mechanisms by which this important gene works.

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Canine cancer immunotherapy studies: linking mouse and human James Fard's says Weerd', James I Madend, Mathed Sterd, Marga Card, Jens Luard, Withen L X. Old', Berl Schard, Web Hand, Jak Margade, Withen J Margade, Mar

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Area:

Immunotherapy

Impact:

In this invited review to a prestigious immunology journal researchers from the medical and veterinary school collaborated in order to compile what is known about the dog as a model of human disease in immunotherapy cancer trials. There have been significant recent advances in the development of immune therapies for human cancer. Traditional mouse models often fail to accurately predict actual response in human patients. There are many similarities between canine and human cancers (much more so than in inducible or transplantable tumors in mice). Ongoing clinical trials are evaluating the potential safety and efficacy of immunotherapies in dogs with naturally occurring cancer. This represents a 'win-win' where our veterinary patients can receive cutting-edge therapies that can potentially also benefit human patients.

Oncotarget, Vol. 3

p73 expression is regulated by ribosomal protein RPL26 th mRNA translation and protein stability Min Zhang^{1,3}, Jin Zhang^{1,4}, Wensheng Yan² and Xinbin Chen²

¹ College of Life Sciences and Technology, Huszhong Agricultural University, Wuhan, China ² Comparative Oncology Laboratory, Schools of Veterinary Medicine and Medicine, University of California at Davi CA, USA

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INTRODUCTION

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Area: P73 Expression

Impact:

P73, a P53 family tumor suppressor, is regulated by multiple mechanisms, including transcription and mRNA and protein stability. Other mechanisms are yet to be explored. In this study, we found that P73 can be regulated by a protein called RPL26. This protein interacts with the messenger RNA encoded by the P73 gene and regulates P73 expression via two distinct mechanisms: protein stability and mRNA translation.



DR5 simultaneous induction and antitumor therapy union New?, Holic New?, Lino V. Wang, Danie Cal', Jolian Dani, Yenhang Zhang, Peng Cheni, Anna X Zou', Janz

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Area:

Drug Resistance

Impact:

An important mechanism of killing tumor cells in the body is through apoptosis – specifically through TRAIL and its death receptors. Targeting these in clinical trials have proven difficult as many cancer cells down regulate these receptors. Using cell lines for lung, breast and prostate cancer we discovered that KDM4A is responsible for this. By inhibiting this protein we can restore TRAIL and the death receptor 5 and sensitize cancer cells to killing.



Area:

Radiation Therapy and Device Development

Impact:

Radiation therapy of the head and neck can result in mucositis and other acute effects in the oral cavity. If we can reduce the radiation dose to parts of the mouth we can reduce side effects. This prospective pilot study evaluated a novel, intraoral, beam-blocking device for use during imaging and radiation therapy. Findings indicate that this novel device can help attenuate radiation dose ventral to the block in dogs with minimal backscatter. We are currently using this in the clinic to reduce side effects for radiation therapy and are designing different size mouth blocks that can be 3D printed so as to allow it to be used in different sized patients.



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Brad Case 2/31, 35	in charact	prize clinical findings, surgical procedures, complications, and in degs underpoing extirpation of macses from the cranial me-			
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Geraldine B. Hunt 375c, 750	in dogs.	ites for case selection when considering VATS for thymectory			
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Michele A. Stelley DVX	2014				
Sarah E. Boston UNM, DVb.	PROCED	URES ords were reviewed and data extracted regarding signalment.			
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		Materials and Methods			
		Case selection criteria			
ABBREVIATIONS ACHR Acstpicholine receptor CHM Crashal mediastinal mass IQR Interquentile range VATS Video-assisted theracic surgery		All dogs that had undergone CMM extirpation from 2009 through 2014 at 5 veterinary academic referra			

Area:

Cranial Mediastinal Masses

Impact:

Tumors located in the chest of a dog can be dangerous and difficult to remove and can result in difficult recoveries. This study describes the use of video assisted thoracic surgery to remove tumors in mediastinum which is located in the thorax in a less invasive manner. One important finding however is that dogs who suffered from secondary myasthenia gravis did poorly and still have a guarded prognosis.

Area:

Thymoma

Impact:

This paper describes low pressure thoracic insufflation facilitated video-assisted thoracoscopic resection of cranial mediastinal masses in a cat with a thymoma which was also causing myasthenia gravis. Thoracic surgery is often difficult in cats with many not surviving long term after more invasive surgical techniques. This newer technique may prove to be safer.



Area:

Osteosarcoma and Metastatic Cancer

Impact:

Clinical research indicates that dogs with bone cancer lived longer when they developed infections at surgery sites. The predominate theory is that this was due to upregulation of the immune system. This work found that the antibiotic used to fight the majority of these infections actually has antitumor activity. It is possible that the addition of this antibiotic may have contributed to improved survival of dogs with bone cancer. More work needs to be done before this treatment can truly be recommended.



"I find gratification in seeing a sparkle in a student's eyes when they see or learn something for the first time. Our residents are the next generation of private practice and academic oncologists and their successes are my legacy as an educator."

– Dr. Katherine Skorupski

Increasing Knowledge Globally

Medical Oncology Residents





Dr. Sami Al-Nadaf

Dr. Rhonda Burge

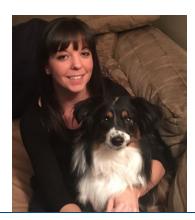


Dr. Marissa Ruppel



Dr. Ji-in Lee

Dr. Sarah Vidal



Radiation Oncology Resident

Dr. Heather Ashcraft

Visiting Scholars

- Dr. Davide Berlato Animal Health Trust, UK
- Dr. Takuya Maruo Azuba University Tokyo, Japan
- Dr. Michael Schmohl Hoffheim Germany
- Dr. Imke Schooper Hoffheim Germany
- Dr. Kyoungwon Seo Chungnam National University Daejeon, South Korea

Visiting Graduate Students

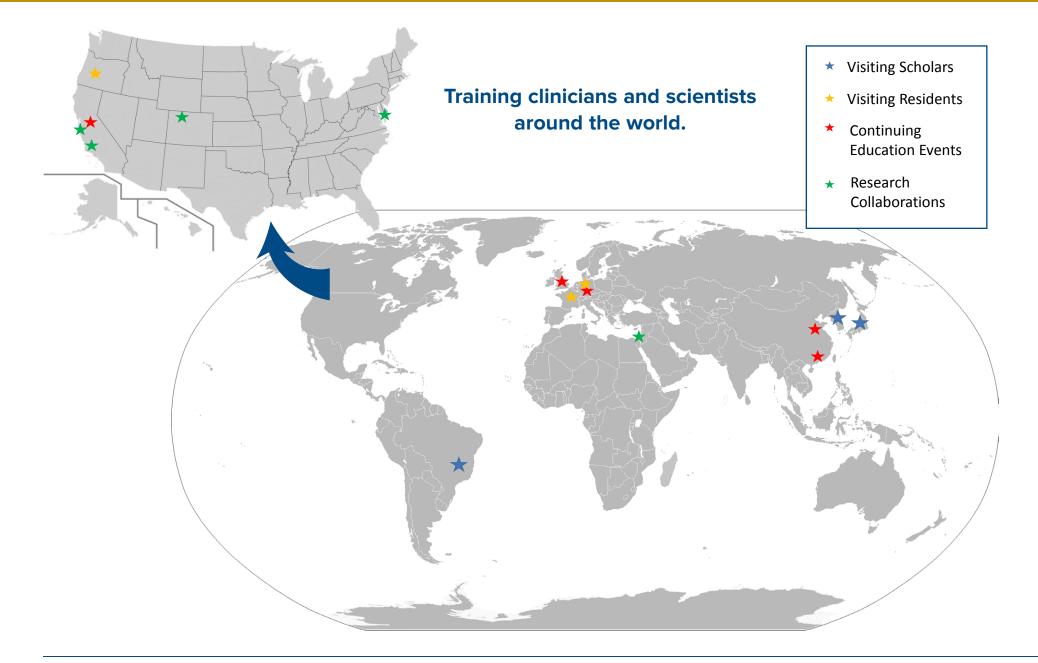
Kazuki Heishima – Gifu University Gifu, Japan

Visiting Residents since 2015:

- Dr. Gabriel Chamel VetAgro Sup Lyon, Lyon France
- Dr. Jason Cuoto Michigan State University
- Dr. Owen Davies Royal Veterinary College, London, UK
- Dr. Antonio Giuliano Cambridge University, Cambridge, UK
- Dr David Sayag VetAgro Sup Lyon, Lyon France
- Dr. Juan Carlos Serra University of Edinburgh
- Dr. Marilia Takada Michigan State University
- Dr. Katja Zimmerman LMU Munich, Germany



Global Connections and Training



Through Collaboration We Can Do More



UC Davis is one of 20 sites that makes up the National Cancer Institute's Comparative Oncology Trials Consortium, a clinical trials group designed to advance cancer research by bringing clinical trials to our dog patients.

Comparative Oncology Program Trials Consortium

Auburn University Auburn, AL

Cornell University

Raleigh, NC

Colorado State University Ft. Collins, CO

West Lafayette, IN Texas A&M University

Ithaca, NY Col Kansas State University The Manhattan, KS Col

North Carolina State University

College Station, TX The Ohio State University Columbus, OH

Corvallis, OR

Purdue University

Oregon State University

University o

Tufts University

Gainesville, FL

North Grafton, MA Guelph,

University of California University Davis, CA Urbana, IL

University of Florida Universit

University of Georgia Athens, GA Guelph, ON Canada

University of Guelph

University of Missouri

Columbia, MO

University of Pennsylvania Philadelphia, PA

University of Tennessee Knoxville, TN

University of Minnesota University of Wisconsin St. Paul, MN Madison, WI

> Virginia Tech Blacksburg, VA

> > Washington State University Pullman, WA



Core Infrastructure and Equipment

"We have been able to invest in setting a biorepository, a pharmacokinetics core, new imaging technologies and are planning for a new imaging facility to support our research and clinical work – ensuring the best for our patients."

– Dr. Michael Kent

A Tissue Biorepository – Banking for the Future

The oncology program recognized the value of storing patient tumor samples to act as a resource for researchers and has started a bank of tumor samples. The biorepository now has over 1,900 samples from over 500 different patients.

Dog Tumor Types Collected:

- Lymphoma, Osteosarcoma
- Oral Melanoma
- Primary Lung
- Hisitocytic
- Mast Cell Tumor
- Soft Tissue Sarcomas

Glioma

Hemangiosarcoma

- Adrenal Tumor
- Synovial Cell
- TVTThymoma

- **Cat Tumor Types Collected:**
- Injection Site Sarcoma
- Oral Squamous Cell
- Carcinoma

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The oncology group has joined the UC Davis virtual biorepository, which makes our biorepository searchable by anyone to promote collaboration and make our samples more accessible to researchers.

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About Us

The Bioanalytical Research Core (BARC) is a unique interdisciplinary analytical core that provides method development and validation for therapeutics and toxicants according to the Food and Drug Administration's (FDA) Compliance Guidelines for Analytical Method Validation.

Our **mission** is to provide expertise in pharmacokinetic/pharmacodynamic (PK/PD) study design, technically advanced instrumentation for detection and quantitation of drug and metabolite concentrations, and pharmacokinetic analyses. We specialize in PK/PD studies at preclinical and clinical stages of drug development specifically targeting oncologic drugs.

BARC's collaborative approach harnesses the expertise of specialists within the School of Veterinary Medicine and the power of collaboration with experts in diverse disciplines across UC Davis, providing an exceptionally rich environment for multidisciplinary investigations. A strong multidisciplinary research infrastructure ensures that sciences will continue to expand in the years ahead.

Our Expertise

BARC Co-Directors Drs. Birgit Puschner and Heather Knych have a demonstrated publication record in the field of pharmacokinetic/ pharmacodynamics relationships and toxicological investigations. They and the laboratory team have advanced training and experience both in the pharmaceutical industry (preclinical drug development) and academia, as well as extensive experience with pharmacokinetic modeling of drug and metabolite concentration data in a variety of biological matrices (blood, urine, milk, synovial fluid, tissue). BARC provides competency in sample extraction, GC-MS/MS, LC-MS/MS analysis and method development.

Collectively, the staff, post-doctoral fellows and faculty members have more than 30 years of experience developing and validating analytical methods for measurement of drug and toxicant concentrations. Faculty members have additional expertise in the field of drug metabolism in numerous veterinary species, specifically with respect to the development and use of in vitro models.

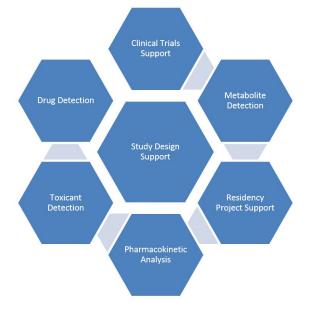
Services We Provide

Data Interpretation

BARC helps researchers capture and understand movement of drugs and toxicants in the body through use of state-of-the-art analytical technologies. We have several previously validated methods for a number of drugs/toxicants and the capability of developing and validating highly sensitive (pg/mL) methods for quantification of novel compounds. We are able to determine drug concentrations in a number of biological matrices including blood (serum or plasma), PBMCs, tumor tissues and DNA.

Analysis

In addition to determination of drug concentrations, we also offer pharmacokinetic analysis services using the industry standard in pharmacokinetic modeling software. Co-located clinical research units enable innovative working collaboration with clinicians, efficient analysis and faster progress of clinical studies.



Bioanalytics Research Core – Pharmacokinetics



Dr. Birgit Puschner, Co-Director

Dr. Puschner received her veterinary degree in 1992 from the University of Munich, Germany. In 1995, she completed her dissertation at the University of Munich, Germany and continued her research interest by joining the University of Michigan as a post-doctoral fellow. From 1996 to 1999 she specialized in veterinary toxicology in a residency training program at UC Davis, which she successfully completed with the Board Examination by the American Board of Veterinary Toxicology. In 2000, Dr. Puschner joined the faculty of the School of Veterinary Medicine at UC Davis and is currently a Professor of Veterinary Toxicology, and Chair of the Department of Molecular Biosciences. She splits her time between teaching and research. Although the past 20 years of her career have been in academia, Dr. Puschner previously practiced both large and small animal clinical medicine and thus, understands what is needed to effectively connect clinical medicine with basic science.



Dr. Heather Knych, Co-Director

Dr. Knych is an Associate Professor of Clinical Veterinary Pharmacology. She attended the University of California, San Diego for her undergraduate work and the University of California, Davis for her DVM and Ph.D. (Pharmacology). She is a diplomate of the American College of Veterinary Clinical Veterinary. Dr. Knych's research focuses on equine drug metabolism and pharmacokinetic/pharmacodynamic (PK/PD) relationships of drugs in performance horses. Additionally, Dr. Knych provides guidance to researchers at UC Davis and other universities as well as to drug companies on PK/PD study design. She assists with drug concentration determination and pharmacokinetic analysis in various biological matrices.



Dr. Ingrid Gennity, Senior Development Engineer

Education:

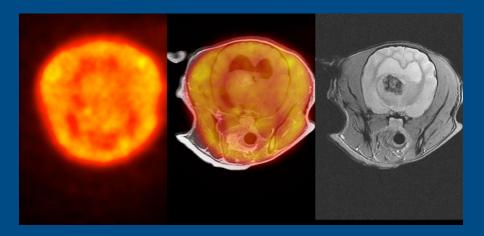
In 1978 she received her M.S. in Biochemistry from Westfälische Wilhelms-Universität Münster in Muenster, Germany. In 1981 she received her Ph.D. in Biochemistry from Westfälische Wilhelms-Universität Münster in Muenster, Germany with a focus on the biosynthesis of unusual lipids and amino acids in plants.



Since animals cannot tell their doctors where it hurts, veterinarians rely heavily on the accuracy of diagnostic imaging to diagnose disease and develop a treatment plan. Imaging is also essential for clinical research — allowing us to see disease, how it progresses and how it responds to treatment. To continue providing the highest standard of care and advance health through research, the School of Veterinary Medicine is committed to staying at the forefront of innovation in imaging technology. In 2015, veterinary radiologists from the school were the first to image a horse using a prototype of a newly created positron emission tomography (PET) scanner that was here to image brain tumors in dogs for a clinical trial. The school permanently acquired the scanner and continues to make breakthroughs in the success of PET scanning — detecting lesions that other advanced modalities (such as CT or MRI) do not identify. Now we are expanding our PET capabilities at UC Davis. On the horizon is the Mini Explorer II project. This next generation PET scanner for imaging small animal patients is under construction and nearly complete, with delivery expected by the middle of 2018. It will provide significant increased sensitivity for total body imaging and perform scans more quickly and with a much lower radiation dose reduced by 40 times the dose currently in use.



First clinical patient in the world to be imaged in the new portable PET scanner. This scanner is also being developed for human use.



PET scan - fused image and MRI of a dog with a glioma, a type of brain cancer that affects dogs and people.

PET imaging allows what is called functional imaging — meaning we can look at the metabolic activity of tissue or areas of hypoxia, which allows us to better identify cancer and its spread. The oncology group has been working with our radiology specialists, biomedical engineers and private industry in developing two new PET scanners. The first is a low-cost portable scanner that has the potential to make PET scanning more accessible and is being developed for people to help in identifying Alzheimer's Disease. The first clinical patient to be imaged with the PiPET system was a dog with glioma (a type of brain tumor) who was involved in a clinical trial. Since then, the scanner has been used to image horse legs to help diagnose lameness.

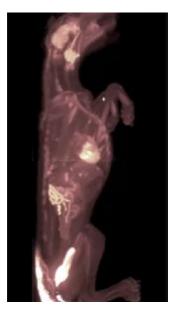
Next Generation Imaging – PET Scanner Development



A dog being imaged in the Mini Explorer I – this prototype was the first iteration of this breakthrough in technology.



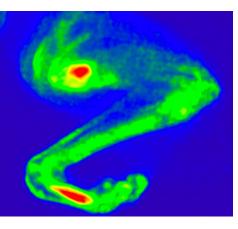
The Mini Explorer II – a combined PET/CT now under construction



PET/CT of a dog

Bringing the Mini Explorer II to the school is the result of a collaborative effort by UC Davis biomedical engineer Dr. Simon Cherry (College of Engineering), medical physicist Dr. Ramsey Badawi (School of Medicine) and the veterinary hospital's Diagnostic Imaging Service. The school's multidisciplinary approach discovers new ways to prevent, diagnose and treat diseases by harnessing the expertise and resources of the entire university behind each veterinarian. "Innovations in diagnostic imaging technology are critical to our school's comprehensive vision for the future," said Dr. Erik Wisner, Associate Director of Diagnostic Imaging.





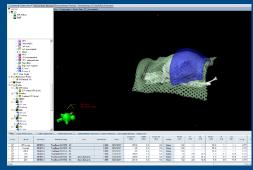
PET scan of a dog with a bone tumor

In radiation therapy, the goal is always to maximize the dose on the tumor and minimize radiation going to normal tissues. One way to do this is to use bolus material for tumors that are near the surface of the body and skin. Boluses act as an artificial tissue that absorb radiation doses. A bolus can be made of many types of materials – such as water-soaked gauze, a modeling compound like Play-Doh, or prefabricated sheets of artificial "skin." None of these are ideal because they do not mold directly to the surface, are not the same density as tissue, and can leave air gaps where the body surface changes shapes. These air gaps interfere with the radiation dose. For example, a flat sheet cannot completely cover a curved part of a body, such as over the nose. After a patient has a CT scan of the area to be treated, a bolus can be "drawn" on the surface. This can then be imported into other software which allows for the creation of a 3D structure which can be printed using a rubbery material that exactly conforms to the patient and is placed on them before each treatment. Each bolus takes

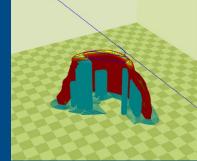
between six and 12 hours to print, depending on the thickness and size. "The 3D printer allows oncologists to make a bolus that is the exact shape as the contour of the patient," said Dr. Michael Kent. "This eliminates air gaps and helps change how the dose distributes to the tissue." To see a timelapse version of the printer in action, please see the "UC Davis 3D Printer Timelapse" video on YouTube. (https://www.youtube.com/watch?v=3mLss6-Seuw).

After researching the best type of material with which to print (that would closely replicate tissue), the radiation oncology specialists print custom boluses for each patient that needs it. Boluses can be printed for just a few dollars each allowing the service to implement this new technology without increasing costs. "This is a great example of how practical translational research can quickly be brought to the clinic and impact our patients," said Dr. Kent.

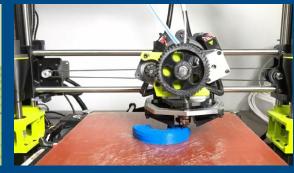
A cat with nasal lymphoma being treated with a 3D-printed bolus.



Treatment planning Image



Computer modeling of bolus



Printing bolus Image



Bolus treatment

Advancements in medical technology are rapidly driving a new age of diagnostic imaging. The veterinary hospital is leading the way in this capacity, and the team is planning an All Species Imaging Center (ASIC) as a hub of the new Veterinary Medical Center. Centrally located in the new facility, the ASIC will bring together radiology, ultrasound, nuclear scintigraphy, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) under one roof to better serve patients and clients. These imaging techniques are critical not just for diagnostics, but to guide the precision therapy clinicians provide to patients. Additionally, imaging is becoming more important in assessing how patients are responding to new treatments. This is vital to our cancer research efforts. "Finding better, less invasive ways of tracking disease and seeing how patients respond to new treatments is vital to improved animal health," said Dr. Michael Kent, CCAH Director.

"The Veterinary Medical Center will be unlike any in the world, one that combines compassionate health care for animals with innovations from across our university, a spirit of discovery and a passion for education that will transform veterinary medicine into the future."

Dr. Michael Lairmore
 Dean and Distinguished Professor
 School of Veterinary Medicine

Rendering of the All Species Imaging Center in the new Veterinary Medical Center Imaging requires cutting-edge equipment and specialized space. Therefore, having a designated area to house this equipment together will streamline patient care. The ASIC will reduce wait and anesthesia times (thus reducing stress on the animal), allow different imaging tests to be conducted at the same time and, above all, promote integrated care and research of the highest quality. The future of imaging at UC Davis will embrace PET scan technology to diagnose injuries that may not be visible with other imaging modalities.

The ASIC will also expand our MRI capability and enable space for a second MRI unit to expand clinical operations and enhance research discoveries. Our clinical and clinical research MRI caseload has steadily increased over the past 15 years, nearly tripling since 2002.





▲ Enzo – Treated in 2012 for jaw cancer – still cancer free.

Advancing the fight against cancer while treating each patient as if they were our own family.



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