

## ESVONC ANNUAL CONGRESS 2025 PORTO PORTUGAL 22-24 MAY 2025

### PROCEEDINGSBOOK

WWW.ESVONC.COM

#### **ESVONC COMMITTEE**

President - Jérôme Benoit Vice-President - Chiara Leo Secretary – Hanne Moberg Treasurer - Neil Palmer Members at Large - Anca Cristea and Juan Borrego Nurse Liaison Officer - Nicola Read

Congress support by the team of Partners in Congress Organisation





#### Message from the President VONC European Society of Veterinary Oncology (ESVONC)

Dear Friends,

This has been an extraordinary year for ESVONC — a year that reminds us of the strength, resilience, and spirit of our community.

At a time when the world feels increasingly divided, when many of us wonder who our true allies still are, it is uplifting to see what WE, as a Society, have built TOGETHER. Our 2025 Congress is sold out, welcoming over 420 participants from across the globe, and we received nearly 100 abstract submissions. This shows a powerful shared need for re-connection, intellectual exchange, and friendship across communities. We are deeply grateful to all our sponsors for their generous support, without which this event would not have been possible.

I would also like to express my sincere thanks to our wonderful local hosts, Andreia, Catarina, and Marta. Their creativity, generosity with their time, and meticulous attention to detail have been instrumental in ensuring that everything runs smoothly during the congress. A special thanks as well to their dedicated team of students, whose support and enthusiasm will be invaluable in assisting all participants throughout the meeting.

Beyond this meeting, our global initiative, under the umbrella of the World Veterinary Oncology Consortium (WVOC), continues to grow. We remain especially proud to support our Ukrainian colleagues, who practice oncology with extraordinary courage and determination. Their resilience is a humbling reminder that our profession offers healing, comfort, and hope, even in the hardest of circumstances.

Closer to home, ESVONC itself is evolving:

- The Nurse Group, led by Nicola Read, is flourishing and preparing to form a dedicated committee to strengthen and grow its activities.
- Our Congress will feature, for the first time, a special "dry-lab" electrochemotherapy session an exciting initiative we hope to develop in future years.
- Our brand new website is now online, offering members a richer library of resources, including recorded webinars and keynote lectures.

None of these achievements would be possible without the incredible spirit of our members and the tireless work of the ESVONC Committee. I am deeply proud of the team working alongside me — year after year, helping to build a Society that is stronger, more vibrant, and more united.

Thank you for being part of our journey. ESVONC is not just a professional network — it is a family. And it is thanks to each of you that we continue to grow, inspire, and make a difference for our patients and their families.

Enjoy Porto and your 2025 Annual Congress! Jérôme Benoit President, European Society of Veterinary Oncology (ESVONC)

## WELCOME TO PORTO

#### "What if we hosted this event in our city?"

This simple question sparked a journey filled with excitement and dedication. It is with immense joy that we welcome this esteemed congress to the beautiful and historic city of Porto. Known for its stunning landscapes, rich cultural heritage and the warmth of its people, Porto offers an inspiring setting for reflection, exchange and innovation.

What unites us is a deep thirst for knowledge and the shared belief that the knowledge should always reach more people. For us, training is the foundation of providing the highest quality care to our patients, by prioritizing education and skill enhancement. Our commitment to organizing and participating in events that foster learning is driven by this mission. Andreia is graduated in Veterinary Medicine from ICBAS – University of Porto and obtaneid her PhD in the field of oncology. She is currently a researcher and professor at the Department of Veterinary Clinics at ICBAS – University of Porto. Catarina holds a degree in Veterinary Medicine at ICBAS – University of Porto and is currently pursuing a clinical research PhD in Veterinary Sciences, focusing on microbiome and immunology field in animals with cancer. Marta is also graduated in Veterinary Medicine at ICBAS – University of Porto, and with an extensive experience in small animal clinical private practice, she is currently part of the team and professor at the Veterinary Hospital of the University of Porto.

Organizing this event has been a true honor. It has been an absolute pleasure for us to bring together all the details, ensuring that every aspect of the event reflects the care, enthusiasm and passion with which we embrace the opportunity to host you here. From the first discussions to the final preparations, it has been a rewarding experience for all involved.

We are deeply grateful for this challenging mission and the opportunity to showcase our city and its vibrant energy. We hope that your time here will be filled with inspiration, meaningful connections and lasting memories. We look forward to the fruitful exchanges and discoveries that lie ahead and we are confident that this congress will be as enriching for you as it has been for us to organize it.

Welcome to Porto, and may this experience be one to remember.

Andreia Santos, Catarina Aluai-Cunha, Marta Teixeira



Welcome Reception - WOW



Congress Venue - Super Bock Arena



Gala Dinner - Bolsa Palace



Dear Colleagues,

It is with great enthusiasm and heartfelt appreciation that we welcome you to our 5<sup>th</sup> ESVONC Nurses Congress. Whether this is your first time joining us or you are a returning attendee, we are honoured to have you here as part of a dynamic, passionate, and ever-growing community dedicated to advancing cancer care for our animal patients.

This Congress is a celebration of collaboration, discovery, and progress. It is also a platform designed especially with you in mind and so over the coming days, we will deliver topics which have been tailored to the unique responsibilities of our roles; from the latest innovations in chemotherapy safety to advanced nursing techniques, client communication, and compassionate palliative care. Every session, delivered to you by our specialist trained, internationally recognised speakers aim to empower you with practical tools and new insights you can take back to your clinics and hospitals.

Equally important, this is a space for connection. Here, you'll find colleagues who understand the emotional highs and lows of our work, who've also sat beside pet parents on tough days, and who share your deep-rooted desire to make a difference. Take time to meet someone new, share stories, ask questions, and contribute your perspective—you are not only learners here, but also leaders and teachers in your own right.

Thank you for the critical role you play in veterinary oncology and for bringing your energy and expertise to this Congress. We hope you leave inspired, recharged, and more deeply connected to this incredible field and the extraordinary animals and people it brings into our lives.

Welcome to the ESVONC Congress—we're so glad you're here!

Warm regards, Nicola Read, Nurse Liaison for the ESVONC Executive Committee



**ESVONC Committees and Task-Groups** 

#### **ESVONC Scientific Committee :**

J. Borrego (Chair)

L. Aresu, N. Bacon, S. Bavcar, J. Benoit, J. Benoit Tanis, P. Bergman, J. Buchholz, J. Burton, S. Carvalho, C. Clifford, M. Clemente, P. Clemente-Vicario, S. Das, O. Davies, I. Del Portillo Miguel, I. Desmas, V. Domingo, J. Elliott, S. Garcia-Pertierra, L. Garret, I. Grant, A. Hayes, J. Henriques, T. Hendrickx, A. Lara García, J. Lawrence, C. Leo, D. Killick, M. Macfarlane, M. Martin, S. Mason, K. McNaught, A. Melendez, H. Moberg, J. Morris, S. Murphy, H. Murua Escobar, M. Parys, D. Perez Alenza, G. Polton, V. Porier, I. Rodriguez, J. Schmit, K. Selting, J. Carlos Serra, M. Tellado, M. Turek, E. Treggiari, D. Vail, M. Zandvliet, A. Yale.

#### **ESVONC Clinical Research Fund Committee :**

E. Teske (Chair), D. Berlato, Q. Fournier, M.C. Nolff and H. Rönnberg

#### **ESVONC Budget Committee :**

L. Beirens van Kuijk and L. van Bergen

#### ESVONC Social Media and Website TG (completed task)

A. Cristea (Chair), T. Hendrickx, and A. Cotitosu

#### **ESVONC Oncology Internship TG :**

C. Leo (co-Chair), I. Grant (co-Chair), A. Hayes, and J. Buchholz

The Executive Committee, on behalf of all our members, extends its deepest gratitude to all our committee members and volunteers for their invaluable time, energy, and dedication to our Society. Your commitment is the foundation of our success, and we are truly grateful for everything you do.



#### **Executive Committee's Report**

#### Recent achievements since 2021

- \* ESVONC 30th Anniversary and a Constitutional Revision (2022)
- \* Veterinary Nurses invited as Associate Members (2022)
- \* Series of task-groups (with dedicated agendas)
- \* The ESVONC Clinical Research Fund (2023)
- \* Educational initiatives including WOC webinars, a yearly nurse program, and hosting the European Radiation Oncology Congress every 3 years (next one in 2027)
- \* Global projects with the newly formed World Veterinary Oncology Consortium (2023)
- \* New logo (2024)
- \* New ESVONC website and Congress App (2025)
- \* Improved presence on Social Media
- \* More professional Office and Congress management support (2025)

#### **Ongoing and future projects**

- \* Oncology Internship Standards in Europe
- \* Forum for clinical studies across European institutions
- \* ESVONC Oncology Nurse Committee
- \* ESVONC Scientific Committee
- \* ESVONC-VCS 2028 joint meeting in Athens, Greece
- \* Expansion of our online library of keynotes and webinars





On behalf of our members and the Executive Committee, ESVONC reaffirms its solidarity with the people of Ukraine. We stand with all Ukrainian veterinary oncology professionals, and the wider veterinary community, who continue their work under unimaginable circumstances. Our thoughts remain with the people of Ukraine, their animals, and all those affected by the ongoing conflict.



#### ESVONC Congress Locations Who is next?

Starting this year in Porto, PCO will assist us in organizing our meetings. As our Society grows and welcomes more attendees, it has become clear that a more professional structure is needed — beyond the incredible dedication of our volunteer Executive Committee members and local hosts, who generously give their time to our cause.

The committee and local hosts remain deeply involved to ensure that every meeting reflects the true spirit of our Society and the hospitality of our hosts. With PCO's support, we aim to deliver the best possible experience for all participants. PCO will oversee the contractual and logistical aspects, including registration, sponsor relations, speaker coordination, venue arrangements, finances, and more.

Our Congress locations are confirmed through 2028, and we will begin accepting new applications next year for the 2029 and 2030 meetings.

As a reminder, the locations and dates recently approved at our AGM are as follows:

Dublin, Ireland – May 2026

Edinburgh, Scotland – May 2027 (joint with the Radiation Oncology group)

Athens, Greece – 2028 (joint with VCS mid-year meeting)



If you would like to proudly contribute to the life of our Society by becoming a local host for one of our future meetings, please contact us at secretary@esvonc.com — we would be delighted to assist and accompany you on this exciting adventure.



#### **ESVONC Clinical Research Fund (CRF)**

One of the objectives of the ESVONC is to promote science in veterinary and comparative oncology, by encouraging and facilitating coordination of research and other contributions to the knowledge related to pathogenesis, diagnosis, therapy, prevention and control of animal tumour diseases.

For this the ESVONC Clinical Research Fund was established in 2022. Its objective is to finance veterinary clinical research projects, including medical and surgical oncology and radiation therapy, for a maximum amount of €5000. Applicants should be a member of ESVONC.

This year only a few applications have been received, which the ESVONC CRF Committee has to evaluate and choose one to be awarded the €5000. The winner will be announced at the ESVONC congress in Porto on Thursday May 22. Considering the low number of applications the committee and the board of ESVONC will look at better ways of communicating about this initiative towards our membership.

Erik Teske

Chair of the ESVONC CRF Committee

This year's Clinical Research Fund is sponsored by Brave Bites





#### World Veterinary Oncology Consortium (WVOC) Update

The World Veterinary Oncology Consortium (WVOC) brings together five leading veterinary oncology societies: JVCS (Japan Veterinary Cancer Society), VCS (Veterinary Cancer Society, North America), ESVONC (European Society of Veterinary Oncology), ABROVET (Brazilian Association of Veterinary Oncology), and AMONCOVET (Mexican Association of Veterinary Oncology).

A dedicated WVOC website is now live and can be easily accessed through our ESVONC homepage *(please visit <u>https://worldveterinaryoncology.com/</u>)* 

The **World Oncology Connections** (WOC) webinars have been a great success and will continue through 2025–26. Each session brings together panelists from the different partner societies to share scientific updates and clinical experiences. The webinars are free to all members of the participating societies and are recorded for later viewing. All past sessions are available on your member's page on our ESVONC website.

In addition, quarterly **Journal Reviews** have been published. For each edition, one volunteer from each society presents a recent article from their region. These reviews are also available on the new WVOC website.

To foster even closer collaboration, the WVOC Committee has agreed in 2023 to organize a **World Oncology Day** once a year, rotating among the annual meetings of our partner societies. This event will feature keynote talks, abstract presentations, panel discussions, and other formats that encourage debate, the exchange of ideas, and broader understanding of different approaches in veterinary oncology.

The first World Oncology Day will take place in Salt Lake City, USA on **September 27th 2025, during the VCS meeting**. The half-day session will focus on **mammary cancers**, with a program chaired by Karin Sorenmo and a selection of invited speakers from around the world.

Jérôme Benoit

WVOC Co-Chair representing ESVONC

Other Co-Chairs of the WVOC: C. Hazelrigg for VCS, M. Guadarama for AMONCOVET, M. Dagli for ARBROVET, T. Kobayashi for JVCS



#### oncology@WSAVA.org

#### EMPOWERING GLOBAL ONCOLOGY: FREE WSAVA RESOURCES FOR ONCOLOGY PRACTICE

Ann E. Hohenhaus, DVM, Diplomate ACVM (Oncology & Small Animal Internal Medicine) Chair, World Small Animal Veterinary Association Oncology Committee Schwarzman Animal Medical Center New York, NY USA

#### WSAVA ONCOLOGY COMMITTEE CANCER RESOURCES

The World Small Animal Veterinary Association Oncology Working Group (WOW), now known as the Oncology Committee (WOC) was founded in 2021 and has a mission to advance oncology care within the global veterinary community through education and awareness of effective and accessible treatments for pets with cancer. No owner should face cancer alone. To meet this international mission, the WSAVA Oncology Committee has focused on creating resources in multiple languages. These resources are all free to download and use to help improve pet cancer care. https://wsava.org/committees/oncology-working-group/

The first resource created by the Oncology Committee was an <u>Oncology Glossary</u> which is useful to both pet owner and members of the veterinary health care team. The document defines over 30 oncology specific terms to help primary care veterinarians and pet owners understand the terms used by a veterinary cancer specialist. Owners of pet with cancer expect their veterinarian to be able to communicate complex information about cancer and this document can help the general practitioner to achieve this goal.(3) This document is the most translated resource and is available in 16 languages.

The newest resource created by the Oncology Committee is the <u>WOC Cancer</u> <u>Surgery Checklist</u>. This document is designed to decrease errors and adverse events, and increase teamwork and communication in surgery. Modeled after the World Health Organization's surgery checklist, the WOC Cancer Surgery Checklist focuses on four time periods in the operative process: before induction of anesthesia, before moving the pet into the operating room, before the skin incision and before the pet leaves the operating room. Surgical checklists are being used more frequently in veterinary medicine.(4) While this version focuses on cancer surgery, it could easily be adapted to any surgical procedure. The WOW/WOC resource with the most variety are the <u>Oncology Fact Sheets</u>. These one-page sheets each focus on one type of cancer. The Oncology Fact Sheets have two versions, one for the pet owner and one for the veterinary healthcare team. The Oncology Fact Sheets give the veterinary healthcare team a fast summary of the treatment options for that particular type of cancer. The companion pet owner version can quickly be printed as a handout for the pet owner to explain the type of cancer their pet has. All Fact Sheets are available in English and some have been translated into Spanish, Portuguese, Chinese, Ukrainian. Eight different tumor types are covered by Oncology Fact Sheets.



WOW/WOC challenges veterinarians to make a diagnosis on our Instagram account, WOWCancerInsights. This Instagram account feature patients from the clinics of WOW/WOC members and helps followers hone their oncology diagnostic skills in just minutes.



Pre-Congress Wednesday 21<sup>st</sup> of May



#### **APMVEAC/GIENOC** Pre-Congress Seminar

09.00-09.30	Opening of Secretariat
09.30-10.15	Al Meets Imaging: Transformative Technologies to impact Veterinary Cancer Management
	Lecturer: <b>Dra. Jessica Lawrence</b> (Surgical & Radiological Sciences; University of California, Davis, USA)
10.15-11.00	Liquid Biopsies: A Revolution in Non-Invasive Cancer Detection / Insights from the Human Side
	Lecturer: Dra. Rosário Pinto-Leite, (Director of Human Genetic Laboratory ULSTMAD – Portugal)
11.00-11.30	Coffee Break
11.30-12.15	The Rise of New Tyrosine Kinase Inhibitors in Veterinary Oncology
	Lecturer: Dra. Jessica Lawrence (University of California, Davis, USA)
12.15-13.00	Cancer Vaccines in Veterinary Medicine: Current Insights and Future Directions
	Lecturer: Dr. Phil Bergman, Veterinary Specialist DVM, MS, PhD, DACVIM (Oncology) (USA)
13.00-13.30	Strengthening Veterinary Oncology Through Community Engagement: The Vital Role of Local/Regional/Global Associations
	Lecturer: Dra. Felisbina Queiroga, DVM, MSc, PhD, University of Trás-os-Montes and Alto Douro, Vila Real

#### **Resident Workshop**

RESIDENTS' WORKSHOP		
15.00-15.45	Principles of Chemotherapy and Clinical Applications	Dr. Dan Gustafson
15.45-16.30	Rationale Approach to Multi-Drug Protocols and Clinical Pharmacokinetics	Dr. Dan Gustafson
16.30-17.00	Coffee break	
17.00-17.45	A review and recommendations Chemotherapy side effects, prevention, clinical approach, and treatment.	Jessica Lawrence
17.45-18.15	General Approaches to cancer pain classification, assessment, pharmacological therapies and other modalities for pain control	Chiara Adami

#### Main Program – Thursday 22<sup>nd</sup> of May

08.00-09.00	Registration	
08.45-09.00	Welcome Esvonc to Oporto	
	Optimizing Cancer Therapy: Predictive Response, Dose Intensity, and Emerging Agents	
09.00-09.30	Prediction of drug response in human oncology based on genomics	Dr. Fernanda Estevinho
09.30-10.15	Drug dose and drug choice: Optimizing medical therapy for veterinary cancer: dosing schemes, novel combinations, and patient-specific dosing or selection of agents	Dr. Dan Gustafson
10.15-10.45	Coffee break	
10.45-11.15	Molecularly Targeted Agents in Veterinary Medicine: Optimal Use of New Drugs Becoming Available to Veterinary Oncology	Dr. Dan Gustafson
11.15-11.45	Revisiting Chemotherapy Dose Intensity and Antibiotic Prophylaxis in Veterinary Oncology: Clinical Impacts and old dogmas	Jessica Lawrence
11.45-12.15	Panel discussion	Speaker Panel
12.15-14.15	Lunch & Poster session	
14.15-14.45	Sponsored talk by IDEXX	Clemence Peyron, DVM, DESV- Médecine Interne
	IDEXX Cancer Dx™: What is it and what do I need to know?	
	This educational session will focus on the innovation and impact of a new diagnostic tool for the early detection of lymphoma in canines, IDEXX Cancer Dx <sup>™</sup> . Attendees will learn the scientific foundation, clinical applications and how this diagnostic tool is revolutionizing veterinary practices by allowing broader access to cancer diagnostics.	
	General abstracts	
15.00-15.12	Genetic Signatures of Therapeutic Response in Canine Cancers	Dawn Duval

15.12-15.24	Using evolutionary constraint to identify functional mutations in the non-coding space of canine osteosarcoma and diffuse large b-cell lymphoma.	Maja Arendt
15.24-15.36	A novel screening platform for personalized molecular targeted therapy in veterinary oncology	Namiko Ikeda
15.36-15.48	Evaluation of whole-body diffusion-weighted imaging for the staging of canine multicentric lymphoma	Laura Barrett
15.48-16.00	A Novel Anti-CD20 mAb for Treatment of Canine B-cell Lymphoma: Pharmacokinetic and Safety Assessment	Andi Flory
16.00-16.30	Coffee break	
	Residents abstracts	
16.30-16.42	Mediastinal lymphoma in 70 dogs treated with lomustine or anthracycline-based multi-agent chemotherapy: a multicenter retrospective study	Diogo Machado
16.42-16.54	Evaluation of a multidrug chemotherapy protocol including alkylating agents for treating canine high-grade T-cell lymphoma	Hannah Versteegh
16.54-17.06	Computed tomography features of salivary glands neoplasia in dogs	Riccardo Finotello
17.06-17.18	Extracellular Vesicles from Canine Hemangiosarcoma Cell Lines as Potential Anti-Cancer Drug Delivery Systems	Yasmine Dadi
17.18-17.30	Preliminary Evaluation of Thalidomide as a Rescue Therapy for Canine Multiple Myeloma	Stefano Ciccarelli
17.30-18.00	ESVONC Clinical Research Fund Sponsored by	ESVONC CRF Committee
	Brave Bites <sup>®</sup>	

19.00-21.00	Welcome Reception	
	Supported by Boehringer Ingelheim	
	Boehringer	

#### Main Program – Friday 23<sup>rd</sup> of May

08.00-09.00	Registration	
	Integrating Palliative Strategies in Veterinary Oncology Practice	
09.00-09.30	Hospice Care in Veterinary Oncology: Integrating Treatment and Palliative Care	Emma Clark
09.30-10.15	Palliative Care in Veterinary Oncology: The Role of Radiation Therapy in Pain Management	Jessica Lawrence
10.15-10.45	Coffee break	
10.45-11.30	Understanding and Managing Cancer Pain in Veterinary Oncology: Beyond Opioid-Based Therapies	Chiara Adami
11.30-12.00	Considerations for End of Life in Veterinary Oncology	Emma Clark
12.00-12.30	Panel discussion	Speaker Panel
12.30-15.00	Lunch and poster session	
13.30-15.00	AGM	
15.00-15.30	Sponsored talk by Hill's Pet Nutrition	Ana Luísa Lourenço - DVM, PhD, Dipl. ECVCN
	The Role of Nutrition in Oncology Treatment	
	Residents' abstracts	Sponsored by vedis Answers You can Frust
15.30-15.45	Defining the mutational landscape in canine oral squamous cell carcinoma	Helia Abdshahzadeh
15.45-16.00	Factors secreted by feline oral squamous cell carcinoma cell lines enhance osteoclastogenesis and resorption, driving bone invasion	Qaisar Tanveer
16.00-16.15	Looking forward to 2026- Presentation	
16.15-16.45	Coffee break	
16.45-17.00	Empowering Global Oncology: Free WSAVA Resources for Oncology Practice	Ann Hohenhaus

	Resident abstracts	Co-sponsored by
		vedis Answers you can trust
17.00-17.12	Radiotherapy as a rescue treatment for Transmissible Venereal Tumour: a retrospective study of 11 dogs.	Maria Teresa Camerino
17.12-17.24	Efficacy and tolerability of intensity-modulated radiotherapy in dogs with heart-base tumours.	Vittorio Botta
17.24-17.36	Acute Ocular Toxicity After Radiotherapy in Canine Sinonasal Tumors	Jonas Brückner
17.36-17.48	Comparative Epidemiological Study of Melanocytic Tumors in Humans, Dogs, and Cats in Portugal	Catarina Alves Pinto
17.48-18.00	Adoptive immunotherapy with cytokine-induced killer (CIK) cells in canine malignant melanoma: an in vitro study	Luiza Cesar Conti
	EVENING TO YOURSELF!	

#### Main Program - Saturday 24th of May

08.00-09.00	Registration	
	Electrochemotherapy in Veterinary Oncology:	
	Mechanisms, Applications, and Emerging Therapies	
09.00-09.45	Electrochemotherapy in Human Oncology: From	Victor Farricha
	cutaneous primary and metastatic tumors to emerging	
	applications in solid tumors	
09.45-10.30	Electrochemotherapy and Immunotherapy: Mechanisms,	Maja Cemazar
	Immunogenic Potential, and Emerging Combinations in	
	Human and Veterinary Oncology	
10.30-11.00	Coffee break	
11.00-11.45	Electrochemotherapy in Veterinary Oncology: Practical	Natasa Tozon
14 45 40 00	Applications and Treatment Optimization	
11.45-12.30	Electroporation-Based Therapies in non-cutaneous	Matias Tellado
10.00.10.00	lumours Denet discussion	Charles Danal
12.30-13.00	Panel discussion	Speaker Paner
13.00-14.30	Lunch boxes will be provided	
14 20 14 42	Anti DD1 and Intratumoral CD2 directed II 2	Dovid Vail
14.30-14.42	Anti-PDT and initiatumoral GDZ-directed ILZ	David Vali
	Vaccination Combination Immunotherapy in Companion	
	Dogs with Malignant Melanoma	
11 12-11 51	Evaluating the impact of elective nodal irradiation for dogs	Patricia
14.42-14.34	with oral malignant melanoma undergoing	Gualtier
	hypofractionated radiotherapy	Ouanier
14 54-15 06	Pharmacokinetics and Safety of Lysine-Specific Histone	Jenna Burton
	Demethylase-1 Inhibitor SP-2577 for Feline Oral	
	Squamous Cell Carcinoma	
15.06-15.18	Evaluation of a therapeutic vaccine against the tumor	Lobke van
	vascular marker versican in dogs with invasive urothelial	Bergen
	cell carcinoma	Ũ
15.18-15.30	Early detection of cancer using circulating tumor DNA in	Benoit Hedant
	liquid biopsies: a first step to improve clinical care of	
	Histiocytic Sarcoma through the follow-up of 30 Bernese	
	Mountain Dogs	
15.30-16.00	Coffee break	
16.00-16.30	Sponsored talk by DeepScan	Dr. Katja
		Kivinen
	DeepScan	
	DeepScan CFD test for cancer treatment monitoring	
	This session will discuss use cases for DeepScan's new	
	CFD test with focus on cancer treatment monitoring.	

	General abstracts	
16.30-16.42	Characterization of somatic mutations in lymphomas of	Valentina
	Bernese Mountain dogs	Granziera
16.42-16.54	Survival outcomes of dogs diagnosed with urethral	Jean-Baptiste
	carcinoma treated with high-dose-rate iridium-192	Eon
	brachytherapy and NSAIDs, NSAIDs alone or no	
	treatment	
16.54-17.06	Staging Findings in Feline Radiotherapy Candidates:	lan Lee
	Incidence and Impact on Treatment Decisions	
17.06-17.18	Reirradiation of recurrent canine intracranial tumors	Maximilian
		Körner
17.18-17.30	IL-12/IL-23 as Serum Biomarkers to Measure Response	Felicia
	and Prognosis in Canine Lymphoma	Westling
20.00	Gala Dinner	
	Supported by Hill's	
	Hill's	
	Transforming Lives	



**Nurses Program** 

#### AEVPORT Pre-Congress Thursday 22<sup>nd</sup> of May

15.00-15.15	Registration (only) Nurse Pre-Congress. Introduction to cancer care.
15.15-15.45	Nicola Read RVN
15.45-16.30	How nurses are and can be more involved in care of the oncology patient. Hugo Oliveira VN
	Chemotherapy administration techniques: understanding what is essential to working safely.
16.30-16.45	Coffee and Comfort Break
16.45-17.30	Ana Costa RVN
	The impact of anesthesia on the cancer patient.
17.30-18.15	Dr. Emma Clark, MRCVS
	End of life care and euthanasia reimagined.

08.00-08.45	Registration	
08.45-09.00	Welcome to the 5th ESVONC Oncology Nurse Conference	Nicola Read & ESVONC Committee
09.00-09.30	Hospice Care in Veterinary Oncology: Integrating Treatment and Palliative Care	Emma Clark
09.30-10.15	Palliative Care in Veterinary Oncology: The Role of Radiation Therapy in Pain Management	Jessica Lawrence
10.15-10.45	Coffee break	
10.45-11.30	Understanding and Managing Cancer Pain in Veterinary Oncology: Beyond Opioid-Based Therapies.	Chiara Adami
11.30-12.00	Considerations for End of Life in Veterinary Oncology	Emma Clark
12.00-12.30	Panel discussion	Speaker Panel
12.30-15.00	Lunch and poster session	
14.00-15.00	AGM	
15.00-15.45	Exploring opportunities for client support mechanisms through pain clinics and the ever- changing world of artificial intelligence	Ana Costa
	Dry Lab Session	
15.45-16.30	ECT – Principles, Application, Case Studies	Matias Tellado
16.30-16.45	Coffee break	
16.45-17.15	ECT - Wet Lab Practical	Sponsors
	Invitation to General abstracts in main hall	
	EVENING TO YOURSELF	

#### Nurses Program – Friday 23<sup>rd</sup> of May

#### Nurses Program – Saturday 24<sup>th</sup> of May

08.00-08.45	Registration	
08.45-09.00	Day 2 of the 5th ESVONC Oncology Nurse Conference	Nicola Read & ESVONC Committee
09.00-09.45	Chemo's Gut Check: Keeping the GI Tract in the Game	Danielle DeCormier
09.45-10.30	From Nadir to Danger: Understanding and Treating Chemotherapy-Induced Sepsis	Danielle DeCormier
10.30-11.00	Coffee break	
	Colleague Case Presentations	
11.00-11.15	Gold standard care for oncology feline patients: Approaches and best practices	Jodie Wilcox and Rebecca Rudolf
11.20-11.35	Electrochemotherapy aftercare	Daniela Andrade
11.40-11.55	Behavioural challenges (the perfect chemotherapy patient)	Abi Bennet
12.00-12.15	The veterinary nurse's intervention in nasal squamous cell carcinoma in cats	Ana Seco
12.20-12.35	Offering support during a patient's twilight weeks	Carrie Harvey
12.45-14.30	Lunch boxes will be provided	
14.30-15.15	When Chemo Goes Rogue: Extravasation Survival Skills	Danielle DeCormier
15.15-16.00	NEW GREEN INITATIVE: Reducing the environmental impact in veterinary oncology	Ana Costa
16.00-16.15	Coffee break	
16.15-16.45	Introducing 2026 in Dublin, Ireland - The continued evolution of ESVONC, shaping future as oncology nurses and technicians	ESVONC EC
	Invitation to General abstracts in main hall	
20.00	Gala Dinner Supported by Hill's	

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A CELEBRAR 20 ANOS

## A CELEBRAR 20 ANOS DE PREVICOX



SOLUÇÕES PARA DOR, INFLAMAÇÃO E MOBILIDADE. CONTACTE O SEU REPRESENTANTE DA BOEHRINGER INGELHEIM PARA MAIS INFORMAÇÕES.

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**Chiara Adami** always had a keen interest for the Academic environment, where she based most of her career from the early postgraduation years until present. She has achieved a PhD in Veterinary Clinical Sciences and she is a Diplomate of both the European (ECVAA) and the American (ACVAA) Colleges of Veterinary Anaesthesia and Analgesia. After having completed her training to become a board-certified anaesthetist at the Vetsuisse Faculty of the University of Berne (Switzerland), she was hired by the same Institution as Clinical Lecturer from 2012 until 2015. In 2015, she was appointed as Senior Lecturer (Veterinary Anaesthesia) at the Royal Veterinary College (University of London), with clinical, research and teaching responsibilities. Her current appointment is Professor of

Veterinary Anaesthesia and Analgesia at the Department of Veterinary Medicine of the University of Cambridge (UK). Pain management and analgesia are her main research interests; at date, her scholarship portfolio comprises about 100 scientific publications between book chapters and peer-review scientific articles.



**Prof. Maja Cemazar** obtained her PhD in basic medical sciences from the University of Ljubljana, Faculty of Medicine in 1998. She was a postdoctoral fellow and a researcher at the Gray Cancer Institute, UK and at the Institute of Pharmacology and Structural Biology, France, as an associate researcher. Currently, she is the Head of Research and Education at the Institute of Oncology Ljubljana and also works as a researcher at the Department of Experimental Oncology. In addition, she is a lecturer in under and post-graduate courses of Cell and Tumor biology, partly employed at the University of Primorska. Her main research interest is in the field of electroporation-based treatments – electrochemotherapy and gene electrotransfer – gene therapy. She is

developing different treatment approaches by utilizing therapeutic genes targeting either tumor angiogenesis or stimulating immune response. Her main objective is also to combine immunomodulatory gene therapy with local ablative therapies, such as radiotherapy or electrochemotherapy. She is actively involved in development and execution of veterinary and human clinical trials on electrochemotherapy and immune based gene therapies. She is a member of different national and international societies and a president of the National Ethical Committee for Animal Experimentation, a vice-president of National scientific committee for deliberate release of the GMO and a President of Slovenian Genetic Society. Her work is also closely related to the involvement of patients into the research and clinical studies by being the elected member of the "Organisation of European Cancer Institutes" OECI board, and Member of the Sub-group on Cancer and member of the Working Group of EU Mission on Cancer. In addition, she serves as a member of Editorial board of several international peer-reviewed journals and is a Deputy Editor of the journal Radiology and Oncology. In 2006 she received the Award of the Republic of Slovenia for important achievements in the scientific research and development in the field of experimental oncology and in 2018 Frank Reidy Award for Outstanding Achievements in Bioelectrics. She was a supervisor of 16 PhD students, and more than 30 BSc theses. She is the author of more than 300 articles in peer-reviewed journals. Her H index is 48.


**Dr. Emma Clark** is the lead veterinarian at Roundwood Pet Hospice, delivering mobile end of life care in the UK.

Dr. Emma qualified from Cambridge in 2001 and worked in mixed practice for 4 years before moving to Wood Street Vet Hospital in North London. It was here that she developed a passion for delivering quality end of life care seeing many patients through from first vaccinations to their final days.

She was a founding team member of the IVC Evidensia telehealth service 2018-2020. In 2021 she joined the Roundwood Pet Hospice

and In-home Euthanasia team as the lead vet responsible for training and service delivery. She is a member of IAAHPC, a Certified Peaceful Euthanasia Veterinarian with CAETA and has a certificate in pet loss support with the Bluecross



Ana Costa graduated as a Veterinary Nurse in 2012 in Portugal where she worked for five years in a small animal hospital. In 2015 she completed her Nurse Certificate in Physiotherapy and in 2017 decided to move to the UK to further improve her knowledge and veterinary nursing skills. After working at the Queen's Veterinary School Hospital in Cambridge, Ana joined the RVC's QMHA anaesthesia team in 2019 where she is been working since. Ana's special interest in anaesthesia led her to ob-tain her Nurse Certificate in Anaesthesia in 2019 and her PgCert AVN in Analgesia and Anaesthesia qualification at the RVC in 2022. Ana is also part of the pain clinic and cardio

thoracic anaesthesia teams. She was also a board member of the Portuguese Veterinary Nursing Association from 2020 to 2022. Ana has been an invited speaker for national and international conferences in the last years and she is the author of two chapters in *The Veterinary Nurses' Practical Guide to Small Animal Anaesthesia* and have published a case re-port, with another one currently under review. Ana has a special interest in pain management, and environmental sustainability and she is passionate about teaching.



**Danielle DeCormier** is a distinguished veterinary professional known for her expertise in oncology and commitment to education. She has been a licensed veterinary technician for over ten years and obtained her VTS in oncology in 2018. As the Director of Clinical Services Education at MedVet, she oversees learning initiatives, manages a scholarship program, and contributes to strategic planning, showcasing her leadership in shaping the future of veterinary technicians. In previous roles, Danielle implemented training systems, organized webinars, and developed oncology

training programs. Her vast teaching and speaking experience reflect her dedication to sharing knowledge. She is the current Director-at-Large for Oncology in AIMVT and lectures internationally on various topics, including chemotherapy, well-being, training, and leadership.

## Fernanda Estevinho

Licenciatura em Medicina pela Faculdade de Medicina da Universidade do Porto -FMUP (1999-2005).

Internato de Ano Comum no Centro Hospital Universitário S. João, Porto (2006).

Internato em Oncologia Médica no Instituto Português de Oncologia do Porto Francisco Gentil (2007-2012).

Pós-graduação em Evidência e Decisão em Saúde, na FMUP (2010). Assistente hospitalar (AH) de Oncologia Médica na Unidade Local de Saúde do Nordeste, e responsável pela Unidade de Oncologia (2012-2014).

AH no Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos (desde 2014 até à atualidade).

AH no Hospital Trofa Saúde Gaia (desde 2015). AH no Trofa Saúde Hospital Central (desde 2023).

Obteve o "Título Experto en Inmuno-Oncología" pela Universidade de Navarra (2020-2021) Doutoranda em Patologia e Genética Molecular no Instituto de Ciências Biomédicas Abel Salazar (desde 2019).

Iniciou programa doutoral em Patologia e Genética Molecular pelo Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto.

Integra a Comissão Científica do Grupo de Estudos do Cancro do Pulmão.

Membro fundador da iOncoCare (International Group for Oncologic Supportive Care Study). Integra a Direção da Pulmonale (Associação Portuguesa de Luta Contra o Cancro do Pulmão), como tesoureira.

Leciona o módulo de oncologia, em Patologia 2, no curso de Enfermagem da Escola Superior de Enfermagem do Porto.

Colaboradora externa da Faculdade de Engenharia da Universidade do Porto

## Victor Farricha

Faculty of medical Sciences of Lisbon - Graduation in Medicine 1993 Hospital EgasMoniz 1994-1995 Residency in Surgery – Hospital Garcia de Orta 1996-2002 Instituto Português de Oncologia (IPO) – Lisbon 2002 – Hospital da Luz - Setúbal 2010 – 2012 Hospital da Luz - Lisbon 2012 – 2020 Hospital lusíadas lisbon 2020-Guest Assistant of the Faculty of Medicine of Lisbon-Surgery since 2008 Graduate assistant in general surgery 2015 Advisory Board Roche-Portugal for Skin Cancer Consultant for Oncológica Sistemas, IGEA Lda, Mirai Medical and Mar Mar Science For Skin cancer and skin metastasis President of the Portuguese Study group for Melanoma and Skin Cancer Head of the Skin Cancer Team of the IPO - Lisbon Active member of the new Portuguese association of Surgical Oncology Author and co-author de 145 communications on cancer treatment modalities Author of 2 Chapters of the Melanoma 2013 book Author e co-author scientific articles in Skin Cancer field International trainer and proctor in the skin cancer area Specific areas of interest: Hypertermia and Electroporation







**Dr. Daniel L. Gustafson** earned his bachelor's degree in Biology from Santa Clara University and his PhD in Cell and Molecular Pharmacology and Physiology from the University of Nevada, Reno. He completed his postdoctoral training in Radiation Biology and Pharmacology at Colorado State University & the University of Colorado Health Sciences Center. Dr. Gustafson spent eight years on the faculty at the University of Colorado Health Sciences Center where he founded the Pharmacology Shared Resource for the CU Cancer Center. He moved to the Flint Animal Cancer Center at Colorado State University in 2007 and currently serves as the Director of Basic

Research for the FACC, co-Director of the Drug Discovery & Development Shared Resource and co-Leader of Developmental Therapeutics for the CU Cancer Center and is the Shipley University Chair in Comparative Oncology. The focus of his research program is cancer therapeutics with a focus on pharmacokinetic and pharmacodynamic determinants of anticancer drug therapy and comparative aspects of these in pre-clinical, veterinary and human clinical oncology. He has been an author on over 190 original scientific articles in journals and over 120 abstracts presented at national and international conferences in the fields of cancer research and pharmacology.



**Dr. Jessica Lawrence** earned her DVM in 2003 from the Ontario Veterinary College in Canada. She completed residency training in Veterinary Radiation Oncology and Veterinary Medical Oncology at the University of Wisconsin-Madison. She is an active Diplomate of the American College of Veterinary Radiology (Radiation Oncology), American College of Veterinary Internal Medicine (Oncology), and European College of Veterinary Diagnostic Imaging (add on Radiation Oncology).

Dr. Lawrence is currently a Professor of Veterinary Radiation Oncology at the University of California, Davis. Previously, she was an Assistant Professor of Medical Oncology at the University of Georgia, Senior Lecturer and Head of Oncology at the University of Edinburgh Royal (Dick) School of Veterinary Studies, and Associate Professor of Veterinary Radiation Oncology at the University of Minnesota. Dr. Lawrence continues to serve as an Adjunct Associate Professor in the Department of Radiation Oncology at the University of Minnesota Medical School. She is a clinician researcher fully engaged in the "One Health" directive as she strives to improve treatment of human and animal cancer and prevention of treatment-related toxicities. She has widely published in comparative and translational oncology, with her research focused on overcoming the immunosuppressive tumor microenvironment and manipulating immune responses to improve tumor radiosensitivity.



**Matias Tellado** graduated from the Faculty of Veterinary Sciences of the University of Buenos Aires in Argentina in 2008. He completed intensive training in small animal medicine at the University of Buenos Aires. He worked as a teacher and researcher in the Biochemistry Department in the same Faculty for eleven years. Matías Tellado is currently director of VetOncologia, a private small animal oncology clinic in Buenos Aires. He completed various postgraduate courses in human and veterinary oncology. He directs and participates in numerous undergraduate and postgraduate teaching activities, including the course in Veterinary Clinical Oncology at the Center for Veterinary Medical Specialties of Buenos Aires (CEMV) and the practical course of electrochemotherapy in veterinary medicine. He is a guest speaker at national and international conferences,

seminars, and congresses in topics related to veterinary oncology and electrochemotherapy. He conducts research in veterinary oncology, mainly in electroporation,

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electrochemotherapy, and gene electrotransfer. Matías Tellado is currently vice-president and founding member of the Argentine Society of Veterinary Oncology (SAOV). Member of the European Association for Cancer Research (EACR) and the International Society for Electroporation-Based Technologies and Treatments (ISEBTT). Member of the Complex Systems Laboratory, Department of Computing, Faculty of Exact and Natural Sciences, UBA. Founding member of the Interdisciplinary Group of Comparative Oncology (GIOnCo).



**Prof. dr. Nataša Tozon** graduated from the Veterinary faculty of the University of Ljubljana in 1991. In 1995, she completed her master's studies and in 1998 she obtained her doctoral degree, defending the doctoral dissertation »The occurence and progression of renal pathological changes in feline immunodeficiency virus-infected cats«. In 2014 she was appointed as Full Professor in field of Animal Health and Diseases – Internal Medicine of Small Animals at the Veterinary Faculty in Ljubljana. Since 1997 she has been lecturing different subjects, primarily infectious diseases and clinical oncology.

She is a member of the Research Programme Group P4 0053, researching endocrine, immune and enzyme responses in healthy and diseased animals and participates in several research projects, primarily in the field of translational oncology and current infectious diseases of dogs and cats.

She also received a special achievement award for research work from the Veterinary Faculty in 2016. Furthermore, in 2017 one of her publications was selected for »Excellent in Science«, which is rewarded by the the Scientific Research Councils of Slovenian Research Agency. She was a mentor to three junior researchers, mentor or co-mentor to 6 postgraduate students (one masters and five doctoral) as well as seven student research studies.

Prof. Nataša Tozon participated in curriculum of Veterinary Faculty in Pisa, Italy and Veterinary Faculty, University of Jerusalem, Israel as an invited lecturer. Since 2007, she has been teaching postgraduate studies in Clinical Oncology – Masters in Oncology at the Veterinary Faculty in Pisa, Italy. As an invited lecturer she also participated in the 1st World Congress in the field of electroporation in year 2015.

Nataša Tozon is a member of the organizing, editorial and program committee of the annual international workshop on the use of electrochemotherapy and gene electrotransfer in veterinary medicine. She frequently participates as an invited lecturer at different types of education in the field of electroporation based therapies around the globe.

In her clinical work she uses her professional experience to successfully transfer knowledge gained from research work to clinical practice. Nataša Tozon is one of the first in the world to introduce some alternative methods of treatment of oncologic diseases, such as electrochemotherapy and immunotherapy employing interleukin-12 gene electrotransfer into veterinary medicine.

#### Thursday 22<sup>nd</sup> of May 14.15-14.45 IDEXX – Clemence Peyron

#### **IDEXX** Cancer Dx<sup>™</sup>: What is it and what do I need to know?

This educational session will focus on the innovation and impact of a new diagnostic tool for the early detection of lymphoma in canines, IDEXX Cancer Dx<sup>™</sup>. Attendees will learn the scientific foundation, clinical applications and how this diagnostic tool is revolutionizing veterinary practices by allowing broader access to cancer diagnostics.

#### Friday 23rd of May 15.00-15.30 Hill's Pet Nutrition – Ana Luísa Lourenço

#### The Role of Nutrition in Oncology Treatment

Nutritional management is increasingly recognized as playing a critical role in supporting cancer treatment in cats and dogs. Clinicians are called to provide nutritional advice and are often dealing with pet owners very motivated to change their animal's diet driven by unsupported information.

Nutritional recommendations in oncology typically focus on three key areas: modification of the tumour metabolism, management of nutritional risk factors, and nutritional support throughout therapy. Ideally, these recommendations should always be guided by species-specific evidence; however, this can be challenging due to the scarcity of well-controlled studies in veterinary oncology. As a result, is frequently necessary to rely on data extrapolated from other species, particularly humans.

This presentation will review the current information available to support informed clinical decisions and optimize nutritional strategies in veterinary cancer patients, with the goal of improving both quality of life and treatment outcomes.

#### Saturday 24<sup>th</sup> of May 16.00-16.30 DeepScan – Dr. Katja Kivinen

#### DeepScan CFD test for cancer treatment monitoring

Circulating cell-free DNA (cfDNA) is a promising biomarker for monitoring the patient's response to therapeutic treatments. We have developed a new cfDNA-based test to monitor cancer treatment response and evaluated it in 55 dogs with cancer and 300 healthy controls. Plasma cfDNA was quantified before the start of the treatment and prior to each treatment cycle in patients, and every three months in healthy controls. cfDNA levels remained stable in healthy dogs, and correlated closely with treatment response in dogs with cancer. The results suggest that our new test works well in monitoring treatment success and cancer recurrence in dogs.

## **Principles of Chemotherapy and Clinical Applications**

## Daniel L. Gustafson, PhD

Professor and Shipley University Chair in Comparative Oncology, Flint Animal Cancer Center, Colorado State University, Fort Collins, CO USA

This lecture will review the basic theories behind treating cancer with drugs. This discussion will include reviewing basic models of tumor growth, the kinetic basic of drug therapy for cancer as well as the curability of disseminated cancer with drugs. The cellular targets of cytotoxic chemotherapy and the cellular processes associated with drug uptake, target engagement and cellular processing of damage and damage signaling will be emphasized when describing the major classes of classical cytotoxic chemotherapy that are commonly used and make up most of drug treatment for veterinary cancers. Specific drug and drug classes described will include the anthracyclines including the synthetic member of this drug class, mitoxantrone. The mechanism of action and clinical use of other antitumor antibiotics, actinomycin D and bleomycin, will be described. Platinum-based chemotherapy drugs will be discussed in terms of their discovery, pharmacology as well as clinical use including the potential use of kidney function as a dosing metric. The antimicrotubule vinca alkaloids vincristine and vinblastine will be described in terms of clinical use and related toxicities. The alkylating agents will be described in terms of those requiring bioactivation as well as specific pharmacological differences within this group of drugs. Drugs that interfere with DNA metabolism, the antimetabolites, will be described including activation pathways and specific characteristics associated with members of this group of drugs. Topoisomerase II inhibitors, the epipidophyllotoxins, and biologics A(L-asparaginase) will finalize this discussion of the group of "classical" drugs commonly used in veterinary practice.

## Rationale Approach to Multi-Drug Protocols and Clinical Pharmacokinetics

#### Daniel L. Gustafson, PhD

Professor and Shipley University Chair in Comparative Oncology, Flint Animal Cancer Center, Colorado State University, Fort Collins, CO USA

This lecture will focus on the scientific rationale for treating cancer with multi-drug protocols beginning with the clinical success of these approaches. The role of tumor cell heterogeneity as well as the concept of negative and positive drug-drug interactions in determining the success or failure of multi-drug protocols will be described. These interactions will include alterations in drug pharmacokinetics including the potential impact of drug transporters. Pharmacodynamic drug responses in multi-drug protocols will be described including the role of additivity, antagonism and synergy in the optimization of drug combinations as well as the concept that independent drug activity may be a more critical component of multi-drug protocol activity than drug interactions. The discussion of clinical pharmacokinetics will be focused on the concept of dose  $\rightarrow$  exposure  $\rightarrow$  response with the understanding that the relationship between dose and exposure is the pharmacokinetic component of doseresponse and the relationship between exposure and response makes up the pharmacodynamic component. Thus, dose-response can be best understood as pharmacokinetic-pharmacodynamic (PK/PD) relationships and that a look at how this is understood in antimicrobial chemotherapy applies to cancer chemotherapy as well. These PK/PD relationships in cancer chemotherapy will be illustrated with descriptions of both toxicity and efficacy endpoints that can be altered by different dosing schema. The lecture will wrap up with a description of pharmacodynamic endpoints in cancer pharmacology and how drug activity may be optimized through an understanding of the PK/PD relationship.

# A review and recommendations Chemotherapy side effects, prevention, clinical approach, and treatment.

#### Jessica Lawrence

DVM DACVIM (Oncology) DACVR (Radiation Oncology) DECVDI (*add on* Rad Onc) Department of Surgical & Radiological Sciences, School of Veterinary Medicine, University of California, Davis, USA

## **Chemotherapy Side Effects**

- Adverse events (AEs) can result during or after chemotherapy administration when treating pets with cancer.<sup>1-3</sup> Successful chemotherapy treatment relies on critical factors, including the pet's age, performance status, co-morbidities, prior and concurrent therapy, and baseline hematologic, biochemical and MDR1 gene mutation status. When these factors are considered, combined with client education and clinician preparedness, serious adverse events can be prevented.
- Knowledge of the chemotherapy drugs prescribed is essential to predict and manage AEs effectively. Normal proliferating cells within the gastrointestinal epithelium, bone marrow, and active hair follicles are most affected by chemotherapy, which causes gastrointestinal signs (nausea, vomiting, diarrhea), bone marrow suppression and alopecia. Additionally, unique AEs are associated with specific chemotherapy agents like doxorubicin (cardiotoxicity in the dog or renal toxicity in the cat) or CCNU (hepatotoxicity in the dog).
- Chemotherapy-induced AEs are categorized into acute toxicities that occur within 24-48 hours of administration, acute delayed effects that occur 2-14 days after administration, or cumulative or chronic toxicity that occurs months to years after treatment. Descriptive AE reporting should follow VCOG-CTCAE v2, which was updated in 2021 to expand the list of potential AEs and include an attribution.<sup>4</sup>
- Acute adverse events (AEs) are usually drug-dependent and include infusion hypersensitivity reactions as well as acute vomiting or diarrhea. Hypersensitivity reactions can be immunoglobulin-mediated (as seen with I-asparaginase) or may arise from mast cell and/or complement activation (as with doxorubicin and paclitaxel). In certain instances (such as with doxorubicin and dacarbazine), administering the injection too quickly may lead to allergic-type reactions, which might improve by slowing the infusion rate. Generally, hypersensitivity reactions should be treated as emergencies requiring prompt intervention. Pre-treatment with antihistamines or steroids may reduce the likelihood of subsequent reactions. Acute vomiting and diarrhea are infrequent but can occur with some medications (like cisplatin and doxorubicin) and may be alleviated with pre-emptive anti-emetics like maropitant and/or ondansetron.
- Delayed acute effects of chemotherapy usually occur 3 to 7 days after administration and often include gastrointestinal toxicity (such as inappetence, nausea, vomiting, and diarrhea) and bone marrow suppression (neutropenia and thrombocytopenia). Cats are particularly likely to develop inappetence and anorexia, and weight should be monitored through hemotherapy. When standard doses of chemotherapy are used, most delayed acute adverse events are self-limiting and resolve within 2 to 3 days without requiring intervention.
- Potential cumulative or chronic chemotherapy adverse events include CCNU-induced hepatopathy or doxorubicin-induced cardiotoxicity in dogs or renal toxicity in cats.

Serial screening for chemotherapyinduced organ dysfunction is generally incorporated into routine monitoring protocols.

Acute tumor lysis syndrome is a unique syndrome that is rarely reported in veterinary medicine and is most reported in association with canine lymphoma. It may develop 24 to 72 hours after treatment and is associated with a significant tumor burden and a rapid response to chemotherapy or radiation therapy. Serum biochemical abnormalities that indicate a diagnosis of tumor lysis syndrome include hyperkalemia, hyperphosphatemia, hypocalcemia, metabolic acidosis, and azotemia. These abnormalities can lead to lethargy, vomiting, diarrhea (often hemorrhagic), bradycardia, neuromuscular weakness, cardiovascular collapse, and shock. Acute tumor lysis syndrome is a medical emergency that requires aggressive management with intravenous fluids and correction of acid-base imbalances.

#### **Clinical Approach to Managing Chemotherapy-Induced AEs**

- Severe chemotherapy-induced AEs are generally rare (≤ 5%), but mild to moderate AEs occur with regularity and are partially dependent on the chemotherapy regimen. Pet owners must understand the risks of chemotherapy and be informed about monitoring their pets for potential side effects. The routine use of client handouts and online resources at the initial chemotherapy consultation educates the pet owner and stresses the importance of home care for the chemotherapy patient. Simple strategies like teaching owners how to check their pet's temperature or advising them to withhold food temporarily for dogs experiencing vomiting or diarrhea can empower pet owners with useful nursing care techniques.
- Because some agents have a higher likelihood of causing clinical signs (e.g., doxorubicin), some clinics may establish routine supportive measures to mitigate nausea, vomiting and diarrhea.<sup>5-8</sup> Measures may include prophylactically prescribing maropitant or ondansetron for the initial days following chemotherapy administration, changing the diet to a gastrointestinal prescription diet, adding prebiotics/probiotics through supplements, and incorporating digestive aids such as hydrated calcium aluminosilicate clay (RxClay or smectite). Crofelemer is a botanical oral medication that normalizes the fluid influx in the gastrointestinal tract. Canalevia-CA1 is a Crofelemer delayed-release oral medication that has been conditionally approved in the U.S. through 2025 for dogs with chemotherapy-induced diarrhea. Clinical evidence is pending to demonstrate its specific role and benefit in routine oncology practice.
- Myelosuppression typically manifests as neutropenia, with chemotherapy drugs commonly causing a neutrophil nadir at approximately 6-7 days. Some drugs like doxorubicin or carboplatin commonly cause late nadirs, and carboplatin can cause a double nadir. Monitoring neutrophil count is prudent to avoid grade IV (severe) neutropenia (neutrophil count < 0.5 x 10<sup>9</sup>/L), as this increases the risk for bacteremia and sepsis. Guidelines for managing neutropenic patients are often practice-dependent. Including multidisciplinary specialists when establishing hospital-wide protocols may be beneficial to ensure compliance and adherence to good antimicrobial stewardship. Most neutrophil counts in dogs will recover within 2-3 days. Antibiotics are generally indicated if the neutrophil concentration is < 0.75-1.0 x 10<sup>9</sup>/L to reduce the risk for bacteremia and sepsis.
- Due to the rise of widespread antibiotic resistance, prophylactic antibiotics are not recommended for preemptive management of diarrhea or myelosuppression secondary to chemotherapy.

- Pets undergoing chemotherapy that present with febrile neutropenia or exhibit sufficiently severe clinical signs warranting hospitalization should receive a thorough evaluation, including a complete blood count, serum chemistry profile, and urinalysis with culture.<sup>1-3</sup> Thoracic radiographs are often necessary for febrile pets to rule out aspiration pneumonia due to regurgitation or vomiting.<sup>1-3</sup> Treatment in-hospital typically consists of IV fluids and antibiotics. Pets displaying severe gastrointestinal signs without fever or neutropenia often require supportive care to maintain proper hydration and alleviate clinical symptoms. Antibiotics are seldom necessary for afebrile, non-neutropenic pets with mild to moderate acute vomiting or diarrhea. However, antimicrobials may be considered in specific cases depending on diagnostic test results and the antimicrobial resistance patterns in the region or hospital.
- Similar to establishing guidelines for managing neutropenia, developing workflows to guide the care of chemotherapy patients that arrive at emergency services for supportive treatment may prove beneficial. Therapeutic protocols can help ensure compliance with intended management strategies and reduce stress for the emergency staff. Prompt treatment for chemotherapy-induced AEs typically results in favorable outcomes, with most pets being discharged within 24 hours of admission.

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# General Approaches to cancer pain classification, assessment, pharmacological therapies and other modalities for pain control

## Chiara Adami

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#### Classification of cancer pain

Pain associated to oncologic disease is complex and involves multiple mechanisms and components. Although acute pain may result from surgery, obstruction and ischemia, based on its duration cancer pain is more often chronic (maladaptive) in nature. Involvement of neural structures causes neuropathic pain, which may be characterised by both peripheral plastic changes and central sensitisation. Organ distension and occlusion determine visceral pain, while involvement of skin, skeletal muscles, bones and tendons/ligaments is associated with somatic pain.

#### Assessment of cancer pain

Assessing and quantifying cancer pain in non-verbal patients can be extraordinarily challenging even for experienced clinicians. Signs are very often non-specific, especially when chronic /maladaptive pain predominates. These signs are difficult to distinguish from symptoms caused by the oncologic disease itself. For example, decreased appetite, nausea and weight loss resulting from gastrointestinal cancer or from therapy may not be necessarily perceived as associated to visceral pain by clinicians. Decreased general activity may be caused by somatic pain; however, it could also be interpreted as the result of deteriorating clinical conditions, tiredness and weakness associated to the oncologic disease. Other nonspecific signs of ongoing chronic pain include altered reaction to touch, excessive licking or self-mutilation, altered demeanour and behavioural changes (aggressivity, depression). More specific signs, namely persistent lameness/diminished weigh and changes in body posture may characterise somatic pain resulting from cancer affecting bones and muscles. Among the methods developed to assess cancer pain, questionnaire-based scales are the most common. They are typically designed to assess the effects of cancer pain on quality of life in dogs. One example of validated and widely used scale is the Canine Brief Inventory in Canine Bone Cancer (Brown et al. 2009); however, many other scales have been described and used.

Quantitative sensory testing (QST) is a semi-quantitative method that may be useful to measure somatic, superficial pain in animals, although in human medicine it is mostly used to diagnose neurological dysfunction affecting the pain pathways. QST relies on the application of mechanical stimulation, via a mechanical algometer, on the affected areas. The applied pressure/force at which a behavioural reaction is evoked, defined as "threshold", is measured and recorded. Although the outcome measure is a numerical variable, this method is considered semi-objective when used in non-verbal patients because the definition of "thresholds" relies on the observer's interpretation of the behavioural response.

#### Pharmacological therapies

Various classes of systemic drugs may be used to treat cancer pain in animals.

• Gabapentinoids (gabapentin, pregabalin)

These compounds decrease central sensitization by inhibiting presynaptic Ca2+ channels in the dorsal horns of the spinal cord. Blockade of Na+ channels and elimination of ectopic nerves activity is part of their peripheral mechanism of action. Although gabapentinoids are commonly used for treating chronic and neuropathic pain, there is limited evidence supporting their use as analgesics. The analgesics properties of gabapentin have been researched with conflicting results in canine pain models other than cancer pain, including disc extrusion and surgical pain. However, one study conducted in dogs with osteosarcoma

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found that the outcome worsened when gabapentin was added to cimicoxib and amitriptyline (Monteiro et al. 2018).

## • Tricyclic antidepressants (e.g., amitriptyline)

These drugs are involved in neuromodulation through various pathways, including inhibition of reuptake of serotonin and norepinephrine, antagonism of voltage-gaited Na+ channels, and antagonism of the N-methyl-D-aspartate (NMDA) receptors. These combined mechanisms help preventing or reducing central sensitization. Although there are pharmacokinetic studies in dog, there is very little evidence of their analgesic efficacy in dogs, as well as very limited information on efficacy, toxicity and side effects in cats. They are a relatively common choice in cases in which the pain syndrome is characterised by both neuropathic and behavioural components (e.g., depression, self-mutilation).

• *N-methyl-D-aspartate (NMDA) receptors-antagonists (ketamine and amantadine)* These drugs act at the level of the dorsal horns of the spinal cord and are used to alleviate pain by decreasing neural remodelling and central sensitization. Reportedly, they also decrease opioid tolerance in humans. There is little evidence of their efficacy in relieving cancer pain.

In conjunction with non-steroidal anti-inflammatory drugs (NSAIDs), amantadine reportedly improved analgesia in dogs and cats with osteoarthritis (OA), a more predictable pain model than cancer pain. However, the lack of suitable formulations, particularly when treating cats, may represent a significant limitation to its clinical use.

Regarding ketamine, this agent is widely used, with or without opioids, and reported as effective in human patients with oncologic disease (Bredlau et al. 2013; Bell et al. 2017). Its intravenous infusion in combination with lidocaine was found effective for palliation of refractory cancer pain in dogs and cats (locolano et al. 2024).

## • Cannabinoids (Cannabidiol oil)

Through activation of CB1 receptors, cannabidiol inhibits release of acetylcholine and glutamate, downregulates dopaminergic pathways, modulates opioids, NMDA and GABA receptors, and decreases inflammation. However, part of the analgesic effects is mediated by the CB2 receptors, which usually are expressed only at low levels in the central nervous system but are rapidly upregulated in both neurons and microglia after injury or inflammation. Pharmacokinetic and toxicity studies have been conducted in dogs and cats, and there is ongoing research in both species that at date have produced limited evidence. While the effects of cannabidiol on epilepsy, behavioural disorders and OA-associated pain have been investigated only in human patients (Lima et al. 2022; Häuser et al. 2023). Cannabidiol oil is available as nutraceutical at various concentrations in many European countries and in in the USA.

## • Opioids

Owing to their analgesic effectiveness, opioids are widely used in humans to manage moderate to severe oncologic pain.

By activating the G protein-coupled receptors, opioids produce a variety of physiological effects including reduced activity of the pain pathways and, ultimately, analgesia. Research has shown that morphine is linked to tumour progression by promoting tumour cell proliferation and suppressing immune responses. The effects of other opioid agents such as methadone and buprenorphine on the immune system, on the other hand, remains less studied, and their potential impact on tumour growth is not yet well understood due to limited scientific research (Pinheiro et al. 2024).

Owing to ethical and legal issues, dispensing and prescribing opioids to animals with cancer is advisable only if they are hospitalised.

## • Tramadol

From legal and ethical perspectives, tramadol may look like an appealing therapeutic option as its oral formulation is marketed for dogs as is suitable for long-term use. Its other major advantage is that, although it shares with opioids part of the mechanism of action, it is not classified as an opioid, which implies easier prescription for non-hospitalised patients and lesser ethical and legal issues. The main active compound is its metabolite, the Odesmethyltramadol, which acts at the level of the serotoninergic and dopaminergic pain pathways.

Despite its practical and logistic advantages, it should be considered that the analgesic efficacy of tramadol is generally regarded as a mild-to-moderate, for which reason it is often used in conjunction with other classes of analgesics to relieve cancer pain. Combined with metamizole, it was found effective for treating chronic pain in dogs (Flor et al. 2013).

#### Local anaesthetics

Besides systemic analgesics, local anaesthetics also play a role in the treatment of cancer pain. Somatic regional/localised pain may be successfully treated with continuous administration of local anaesthetics via perineural or epidural catheters. While the use of catheters usually require hospitalisation, nerve alcoholization techniques with phenol, when applicable, may represent a useful and effective way to provide palliative care in terminal cancer patients on the medium-term.

## Non-pharmacological modalities for pain control

Physical therapy and acupuncture may be used as complementary treatment options in animals suffering from cancer pain.

Regarding acupuncture, this will be discussed more in details during the second lecture. Although the literature pertaining to its effectiveness to treat cancer pain in animals is scarce, recent systematic reviews indicated that acupuncture improved pain relief in human patients with oncologic disease (He et al. 2020; Yang et al. 2021).

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## THEMED SESSION – Optimizing Cancer Therapy: Predictive Response, Dose Intensity, and Emerging Agents

## Prediction of drug response in human oncology based on genomics

Fernanda Estevinho

## Drug dose and drug choice: Optimizing medical therapy for veterinary cancer: dosing schemes, novel combinations, and patient-specific dosing or selection of agents

## Daniel L. Gustafson, PhD

Professor and Shipley University Chair in Comparative Oncology, Flint Animal Cancer Center, Colorado State University, Fort Collins, CO USA

This lecture will focus on the variability in drug pharmacokinetics (PK) and pharmacodynamics (PD) in the use of drugs to treat cancer in veterinary oncology. The discussion will include a description of the sources of variability in oral dosing of drugs as well as complications associated with multiple drug dosing. This will focus on time invariance and how changes in body composition and drug metabolism may change drug exposure over the course of patient treatment. Other sources of variability including drug interactions with supplements and other drugs as well as physiologic, biochemical and environmental contributors to variability in the dose-exposure (PK) relationship. A discussion of drug choice will describe how drug choice can be affected by either considerations of toxicity or efficacy and how response varies across tumors. A discussion of biomarkers and the importance of them in drug efficacy and choice will be presented looking at molecular biomarkers including MAPK signaling signatures and ErbB2 in canine bladder cancer. The use of genomic signatures in drug selection will conclude the lecture with a description of the identification and application of algorithms to predict drug response in cell lines and the application of this approach to a clinical trial in dogs with osteosarcoma. This discussion will highlight the importance of prospective testing of prediction algorithms and how validation in patients is critical prior to use.

#### Molecularly Targeted Agents in Veterinary Medicine: Optimal Use of New Drugs Becoming Available to Veterinary Oncology

## Daniel L. Gustafson, PhD

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This lecture will describe the development of kinase inhibitors as a drug class for the treatment of cancer and the current state of the use of kinase inhibitors in veterinary medicine. A focus on the therapeutic development of kinase inhibitors will describe target identification, cell line verification and screening, safety and PK in dogs with cancer and the eventual testing of targeted agents and identified biomarkers in veterinary cancer patients. Examples of target identification will be discussed as well as the use of genomic analysis and phenotypic screens to identify potential therapeutic agents in the absence of obvious drug targets. The safety and PK of targeted agents in dogs will be discussed using the example of trametinib where the use of the proper pharmaceutical product is critical to reliable exposure in veterinary patients. Safety, PK and clinical testing of vemurafenib and lapatinib in veterinary patients will be discussed highlighting the successes and failures associated with the use of these drugs. The discussion will conclude with a summary of how veterinary oncology should proceed in bringing these drugs to clinical use in the most optimal manner.

## Revisiting Chemotherapy Dose Intensity and Antibiotic Prophylaxis in Veterinary Oncology: Clinical Impacts and old dogmas

#### Jessica Lawrence

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## **Chemotherapy Dose Intensity**

- Cytotoxic chemotherapy is typically administered at the maximum tolerated dose (MTD) on a specific schedule, aiming to balance tumor control with acceptable toxicity.<sup>1</sup> Significant effort is required to determine dose schedules that maximize the benefit-to-toxicity ratio, especially for multi-agent protocols.<sup>2</sup> Determining the intent of chemotherapy is also vital to defining an acceptable toxicity profile.
- Relative dose intensity (RDI) is defined as the ratio of the delivered dose intensity to the planned dose intensity for a chemotherapy regimen. RDI is defined as the dosage of drug per unit body surface area per time (mg/m<sup>2</sup> per week), and it can be used as a summary measure to document dose delays, dose reductions, and/or non-adherence within a chemotherapy protocol.
- Clinical evidence from human oncology supports that higher RDI is associated with improved overall survival, progression-free survival, and disease-free survival for patients with solid tumors and lymphoma, while lower RDI is linked to shorter outcomes.<sup>3,4</sup> Although there are nuances to the chemotherapy regimen and underlying tumor histology, an RDI of less than 85% is considered a clinically significant reduction from standard or planned therapy for solid tumors. An optimal RDI for hematopoietic tumors like non-Hodgkin's lymphoma is less clear but is likely near 85-90% for patients with good performance status. Prophylactic treatment and patient education are routinely incorporated into treatment protocols to maintain RDI.
- The significance of RDI is unclear in veterinary oncology, where there is a substantial need to balance the likelihood of long-term tumor control with minimal significant toxicity.<sup>5</sup> Several studies suggest that dogs with lymphoma that experience dose delays and/or reductions following neutropenia have improved remission durations and outcomes. This may support the idea that a tailored dose-dense protocol may be warranted rather than a focus on an intended dose intensity.
- Dose delays and reductions are standard methods of mitigating the chemotherapyinduced side effects of treatment. Neutropenia is a primary dose-limiting adverse event (AE) associated with chemotherapy, and febrile neutropenia can result in hospitalization, discontinuation of treatment and rarely death.
- Establishing neutropenia guidelines for chemotherapy administration and monitoring and managing neutropenic events may be an effective means of maintaining or improving RDI. Pretreatment absolute neutrophil concentration cutoffs for safe administration vary widely between institutions and clinicians, ranging from ≥1.5 × 10<sup>9</sup>/L to ≥2.5 × 10<sup>9</sup>/L.<sup>6</sup> Similarly, there is no uniform consensus for dose reductions, and empirical dose reductions of 5-25% may be made following a chemotherapy AE.<sup>7</sup> Practice-specific guidelines unique to the oncologic team and drug protocol are recommended until such consensus is made.

## Antibiotic Prophylaxis in Veterinary Oncology

- Antimicrobial stewardship by veterinarians preserves antimicrobial drugs' effectiveness and availability through conscientious decision-making and diligent oversight. Due to the rise of widespread antibiotic resistance, prophylactic antibiotics are not routinely recommended for pre-emptive management of diarrhea or myelosuppression secondary to chemotherapy. However, the use of antibiotics has a role in limiting serious AEs following chemotherapy.
- Unlike human oncology, veterinary oncology has operated without formal prophylactic antibiotic guidelines. Reported neutropenia thresholds triggering prescription for antibiotic prophylaxis have ranged from <1.5 x 10<sup>9</sup>/L to <0.75 x x 10<sup>9</sup>/L.<sup>8</sup> Reducing the threshold to the minimum acceptable level will reduce the use of unnecessary antimicrobial use. It is essential to recognize that neutrophil concentration does not necessarily correlate to neutrophil function, and some dogs may become ill despite adequate neutrophil values.
- When prophylactic antimicrobials are used, the choice of drug and duration of treatment are important considerations. To reduce disruption of the gut microbiome, it is recommended to select antibiotics that are effective against Gram-negative bacteria but spare anaerobic flora. Gram-negative bacteria are more likely to translocate and cause sepsis in chemotherapy patients. Trimethoprim-sulfadiazine (TMPS) is ideal for most dog breeds without hepatic dysfunction, as the duration of treatment is short. Fluoroquinolones can be considered in pets that cannot receive TMPS. Antibiotic choice should be tailored to individual pet factors, local antimicrobial resistance patterns, and locoregional guidelines that are publicly available. The duration of treatment should be limited to the point of neutrophil recovery and ideally requires repeated neutrophil assessment.
- In human oncology, antibiotic resistance is linked to shorter outcomes than patients without resistance pathogens.<sup>9</sup> Equal data in veterinary oncology are lacking, but future studies could address this.
- The gastrointestinal microbiome can affect gut function, metabolism, immune response, and possibly tumor response to treatment. Since chemotherapy and other anti-cancer therapies can also disrupt the gastrointestinal microbiome, additional research is needed to understand the potential interactions between antibiotic-induced dysbiosis and therapy-induced effects.
- The inclusion of multidisciplinary specialists may support the development of protocols that incorporate antibiotic use in veterinary oncology.

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## THEMED SESSION –Integrating Palliative Strategies in Veterinary Oncology Practice

## Hospice Care in Veterinary Oncology: Integrating Treatment and Palliative Care

#### Dr. Emma Clark MRCVS

Learning objectives:

- 1. Understanding how palliative care permeates through standard oncological care and when it becomes hospice care
- 2. Awareness of the importance of caregiver communication and support to ensure patients receive contextualised care at the end of life
- 3. Establishing the benefits of hospice care not only for the patient but for the caregiver and the veterinary profession as a whole.

#### 1/ What is palliative care and why is it important in oncology?

Palliative care concentrates on alleviating pain and discomfort for a life threatening condition at any stage of life. The field of veterinary oncology by its very nature often deals with life threatening conditions. Viewed through the lens of the patient, this creates a natural synergy between oncology and palliative care. For the patient this extends life expectancy and aims to improve quality of life for weeks, months or even years. For the caregiver it drives positive outcomes in mental health and return rates to clinics.

For many oncological patients, palliative care is given alongside curative treatment or as a stand alone therapy, such as metronomic chemotherapy or palliative radiation. It includes conventional medicine, complementary therapies such as nutrition, acupuncture, and physical therapies as well as environmental adjustments. These combine to provide pain relief, symptom management and physical support.

#### 2/ The importance of caregiver communication and support

Excellent communication and support is needed to prepare families so that they can make an informed decision about their pet's care with the help of the oncology team.

Best practice is to provide contextualised care by taking into account patient & client specifics. A detailed plan provides clear communication around prognosis, disease progression, and treatment options. This includes:

- 1. Exploring their previous experiences with end of life care and assessing their ability to cope with the demands that may be put on them.
- 2. Providing high quality hospice care at home. The success of the in-home service depends on three caregiver factors: their quality of life, their caregiver burden and their level of anticipatory grief.

3/ The benefits of hospice care for the patient, caregiver and the veterinary profession Hospice care is palliative care at the end of life when a terminal diagnosis has been made, where treatment is no longer beneficial, where caregivers have decided against continuing with a curative course, or simply need some time to adjust to the reality of euthanasia.

Good hospice care benefits not only the patient, but also the caregiver and the profession as a whole.

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## Palliative Care in Veterinary Oncology: The Role of Radiation Therapy in Pain Management

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## Palliative Radiation Therapy:

- Palliative care focuses on providing comfort and support for pets with advanced disease.<sup>1</sup> It often involves an interdisciplinary approach to managing pain, clinical symptoms, and systemic stress caused by cancer.<sup>1,2</sup> The primary goal is to maximize the quality of life for pets with cancer. Palliative care is distinct from hospice care and is suitable for pets of any age and at any stage of disease.
- Radiation therapy is an effective modality for pain relief in cancer care and, therefore, has a prominent role in the management of advanced cancer. Its ability to reduce pain is well supported in comparative literature.
- Early integration of palliative radiation therapy can improve survival times in human and veterinary oncology. It may be prescribed in parallel with other definitive treatments; however, potential long-term complications of palliative intent radiation therapy must be considered.
- In veterinary oncology, palliative intent radiation is commonly prescribed for primary bone tumors, metastatic lesions to bone, tumors impairing normal function (e.g., urinary outflow), and painful tumors in any location. Combining radiation therapy with other treatments may further improve pain outcomes.<sup>1</sup>

#### Mechanisms of Radiation-Induced Analgesia:

- Cancer pain may be caused by local or metastatic tumor invasion into tissue, remodeling of the tumor microenvironment, direct nerve root invasion or compression, and an increased release of inflammatory mediators that stimulate nerve fibers. In humans, bone pain is the most common source of cancer pain.
- The exact mechanism of radiation-induced pain relief remains unclear. Pain palliation with radiation therapy is likely multifactorial, inducing analgesia through the direct destruction of tumor and inflammatory cells, modulation of the tumor microenvironment, and potential disruption of pain signaling pathways. Pain control often occurs before, or in the absence of, observable tumor shrinkage, and some pets will experience rapid pain relief, likely secondary to decreased inflammatory cell activity.
- Data from the use of low-dose (10-20 Gy) radiation therapy for painful benign lesions in humans has also shed light on possible mechanisms of action for low-dose radiation treatment.3 Effects of low-dose radiation are likely influenced by total dose and fraction size. For example, low total doses (2-6 Gy) and low dose per fraction (< 1 Gy) have anti-inflammatory effects, whereas total doses in the range of 8-10 Gy with fraction sizes 1.5-3 Gy likely inhibit fibroblast proliferation. The potential risks versus benefits must be considered when prescribing radiation for non-neoplastic diseases, particularly when long-term control is possible.

## **Palliative Radiation Therapy Protocols**

- Various radiotherapy regimens can be used in pain management. Conventional
  radiation therapy protocols have traditionally been used to maximize the chance of
  tumor control while minimizing the likelihood for unacceptable toxicity. In veterinary
  medicine, these protocols generally involve 15-20 fractions of radiation using a low
  dose (<3 Gy) per fraction. In a palliative setting, hypofractionated radiation protocols
  are typically used to reduce the number of anesthetic episodes and limit time away
  from home.</li>
- Depending on the protocol, radiation can be delivered once or twice weekly or daily. In some cases, a single fraction of radiation may be indicated.
- An "optimal" palliative-intent radiation protocol has not been defined and is probably dependent on tumor type, anatomic location and patient performance status. In human oncology, some clinical practice guidelines based on published literature exist to aid in evidence-based decision-making.
- Both human and veterinary studies demonstrate that radiotherapy provides effective pain palliation with similar strong (70-80%) subjective response rates across species.1,2 However, response duration is variable and difficult to predict.

## **Palliative Radiation Therapy Techniques**

- Traditional palliative regimens, including much of what is reported in the veterinary literature, involved the use of clinical (manual) setups or 3-dimensional conformal radiation therapy (CRT).<sup>1</sup>
- Significant advances in radiotherapy planning, like intensity-modulated radiation therapy (IMRT) or volumetric modulated arc therapy (VMAT), and image-guided delivery may improve outcomes for pets treated with palliative treatment. Stereotactic ablative body radiation therapy (SABR or SBRT),4,5 which employs high (ablative) fraction sizes given daily or every other day combined with precise and accurate radiation delivery, has allowed dose escalation for many tumors.
- Extrapolating from human oncology, SABR may augment response durability and survival time for some patients with bone metastasis.2,4 However, key gaps in knowledge remain regarding optimal fractionation, patient selection, and treatment modality. The likelihood for re-irradiation must also be considered when determining initial fractionation schemes.<sup>6</sup>
- Evaluating pain in radiation therapy studies is challenging, and most veterinary literature reports local control and subjective quality of life changes following palliative intent therapy.7,8 Carefully controlled prospective studies incorporating objective pain measures are ideal for comparing the anti-pain efficacy of various regimens.

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## Understanding and Managing Cancer Pain in Veterinary Oncology: Beyond Opioid-Based Therapies

## Chiara Adami

Professor in Veterinary Anaesthesia and Analgesia, University of Cambridge

#### Pain mechanisms

Neoplastic invasion of healthy tissues and vascular structures, disruption of local vascularization, vasospasm, ischemia, and both chronic and acute inflammation can all contribute to cancer pain.

As a result, oncologic pain is a complex model that may comprise multiple components and is characterised by high inter-subject variability even within the same type of oncologic disease.

## • Neuropathic pain

Mechanisms that can specifically lead to neuropathic pain may be central or peripheral. The latter are usually associated with an injury of the peripheral nerve structures, and include perineural invasion by the growing tumour, peripheral nerve damage/sensitization, and upregulation of heterotopic Na<sup>+</sup> channels (Paice 2003).

Central sensitization can determine neuropathic pain via activation of both the  $\alpha$ -amino-3hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) and the N-methyl-D-aspartate (NMDA) receptors, astrocytes activation and, ultimately release of neuropeptides and cytokines (TNF, IL-1 $\beta$ , IL-6, ATP and CCL2) that augment neurogenic inflammation.

In humans, recent research identified the Botulinum toxin type A as an important coadjuvant in the treatment of several types of cancer, to diminish pro-tumour activity and secondary pain (Reyes-Long et al. 2021).

## • Radiotherapy- and chemotherapy-induced

Vincristine has the potential to cause upregulation of the Ca<sup>2+</sup> channel ( $\alpha$ 2 $\delta$ -1 subunit) in the dorsal horns of the spinal cord, enhancing nociceptive signalling and contributing to central sensitization (Li et al. 2025). In addition to this, vincristine- and radiation therapy-induced neuropathies and plexopathies have been reported in people (Mosa et al. 2025). Other effects of chemotherapy and radiotherapy that may contribute to pain are inflammation, particularly mucositis, ischemia, and fibrosis.

## • Cancer-induced bone pain (CIBP)

Cancer-induced bone pain is well characterised in both humans and murine models. Despite the paucity of literature pertaining to CIBP in dogs and cats, it is reasonable to assume that these species may also be affected. Mechanisms contributing to CIBP are loss of bone mineral density, osteolysis, and cancer-induced bone remodelling, with pathologic osteoclastic bone reabsorption being the primary genesis, maintenance and exacerbation of bone cancer pain (Wang et al. 2025).

The periosteum and medullary cavity are the bony structures with the greatest density of afferent nociceptors, while non-neoplastic stromal cells amplify the inflammatory cascade through release of chemical mediators.

Although this type of pain is better characterised as chronic pain phenotype, reacutization may also occur, triggered by pathological fractures and inflammation.

## Advanced interventional pain treatment

Refractory pain that responds poorly to conventional pharmacological treatment may be addressed with alternative therapy options. Although the latter play a pivotal role in the management of terminally ill patients as part of their palliative treatment, they may also be used to improve quality of life prior to chemotherapy or radiotherapy.

## • Neurolysis

Neurolysis consists of intentional injury to a nerve or group of nerves using chemical, thermal, surgical, or cryogenic methods. In terminally ill humans, neurolysis reportedly improved survival and quality of life (Christo et al. 2008).

Chemical neurolysis with phenol is the most popular technique, although other neurolytic agents such as alcohol and glycerine may also be used. Although these procedures are performed in animals under general anaesthesia, since the initial phase of neurolysis can cause inflammation and discomfort, the chemical agents are usually mixed with a local anaesthetic, typically bupivacaine. Neurolytic agents predominantly affect neuronal axons rather than neuronal bodies. The effects of chemical neurolysis are transient and last for approximately 3-6 months. Thereafter, axonal regeneration and neural plasticity may cause reoccurrence of the pain syndrome (Ben Aziz et al. 2025). In order to increase the chances of successful neurolysis and reduce the procedural risks, it is important to avoid blind techniques and perform an either ultrasound- or fluoroscopy-guided (depending on the anatomical characteristics of the target area) injection of the chemical agent (Ben Aziz et al. 2025).

Besides the treatment of neuropathic pain arising from the tumoral invasion of nerve structure, in human medicine another common indication for therapeutic neurolysis is the alleviation of visceral pain associated with gastro-intestinal and abdominal cancer (Sato et al. 2025)

Risks associated with therapeutic neurolysis are neuritis, neurological deficits affecting sensory and/or motor function, and iatrogenic damage to peri-neural tissue such as inflammation and necrosis.

Because neurolysis is a procedure that implies risks and additional costs to the management of cancer patients, it may be useful to perform a prognostic local anaesthetic block of the target nerve prior to proceeding with the actual administration of the neurolytic agent.

## • Perineural and neuraxial catheters

Perineural and neuraxial (either intrathecal or epidural) catheters may be very useful to provide medium-term analgesia. Although these catheters are designed to be left in place for weeks, the main challenge that we face in veterinary medicine is that, owing to difficult athome management and increased risk of infections, they are generally considered more suitable for animals that are hospitalised. Moreover, unlike neuraxial catheters which, once secured, tend to stay in place, perineural catheters are easily dislocated.

Regarding neuraxial catheters, one way to reduce the risk of contamination of the catheter port and of subsequent infection is the use of implantable drug delivery systems connected to the catheters. Implantable drug delivery systems are battery-powered programmable pumps equipped with remote control. In humans, they are typically implanted subcutaneously in the anterior wall of the abdomen, and connected to the catheter after the latter is tunnelled across the flank (Heo et al. 2014). Pain management through implantable drug delivery system reportedly increased survival and improved quality of life in cancer patients. (Christo 2008). Although promising, the management of neuraxial catheters in non-hospitalised animal patients remains a cause of concern, also considering that the choice of drugs administered through the catheter is influenced by ethical issues.

## **Complementary treatments: Acupuncture**

Acupuncture consists of the insertion of solid needles in specific areas of the body, named acupoints. It has been used for thousands of years to treat various conditions across multiple body systems; however, in veterinary medicine and particularly in the Western world pain syndromes remain its most common indications (Lai et al. 2025).

Acupuncture is becoming increasingly popular in veterinary medicine, fuelled by the growing interest of pet owners in complementary and alternative therapies.

The Western approach to acupuncture focuses on identifying and treating trigger points specific areas of the body that are highly sensitive to stimulation. In contrast, traditional Chinese medicine takes an entirely different perspective, organizing the body into meridians and interconnected systems to guide treatment.

Research has demonstrated the neurophysiological effects of acupuncture in humans, including interactions with the endogenous opioid system, spinal modulation of pain signals through non-noxious stimuli, and anti-inflammatory responses at various levels—local (needling site), segmental (dorsal horn of the needling site), hetero-segmental (across spinal segments), and within the brain (Theysohn et al. 2014). Studies in human medicine indicated that acupuncture improved pain relief in human patients with oncologic disease (He et al. 2020; Yang et al. 2021). However, as of now, published evidence on its effectiveness in animals—particularly in Western countries—remains limited, particularly with respect to cancer pain.

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## **Considerations for End of Life in Veterinary Oncology**

## Dr. Emma Clark, MRCVS

Learning objectives:

- 1. Understanding the unique human-animal bond for each family to tailor the treatment pathway for that patient
- 2. Familiarity with the four key budgets faced by each family: financial, emotional, physical and time constraints
- 3. Recognising the benefits of hospice care in minimising feelings of guilt, regret and remorse.

#### 1/ Understanding the importance of the human-animal bond in care

Veterinary teams are privileged to witness the strength and unique nature of the human animal bond on a daily basis in their work lives. This bond is an interconnected and dynamic relationship where humans and animals benefit mentally, physically and emotionally. By providing empathetic care, the treatment plan can be adjusted to each family's situation. This maximises compliance from both the pet and the caregiver and ensures that patients receive the treatment they deserve at the end of life.

However if the human-animal bond becomes strained this can lead to an accelerated decline in the patient and a premature euthanasia decision. This leads to frustration & moral distress for the veterinary team.

#### 2/ Four key family budgets that affect care decisions

Families face four key challenges: financial, emotional, physical, and time constraints. They influence families' ability to provide end-of-life care.

Understanding all four of these factors allows customisation of treatment plans that align with each family's situation so that contextualised, patient-centered care can be delivered that respects their unique needs.

#### 3/ How hospice care can minimise feelings of guilt, regret & remorse

When considering end of life care, quality of life should be continually assessed so a euthanasia decision is made in a timely manner. Families' previous experiences, their expectations and details of their support network are key to preparing a meaningful and peaceful last moment for their pet. This minimises feelings of guilt, despair and regret. So whether fighting to save a life, cure a cancer, or palliate a patient, the key guiding principle is to respect and support the profound human-animal bond for each and every patient.

## THEMED SESSION – Electrochemotherapy in Veterinary Oncology: Mechanisms, Applications, and Emerging Therapies

# Electrochemotherapy in Human Oncology: From cutaneous primary and metastatic tumors to emerging applications in solid tumors

## 16-Year Experience with Over 1000 Patients Treated at IPO Lisboa

## Victor Farricha

# 1. What is Electrochemotherapy (ECT)? – Biological Principles and Technical Foundations

Electrochemotherapy is a localized cancer treatment that synergistically combines a chemotherapeutic agent (most frequently **bleomycin**, sometimes **cisplatin**) with brief electric pulses applied directly to the tumor area. These pulses induce **reversible electroporation**, a transient increase in the permeability of the cancer cell membrane, allowing cytotoxic drugs—otherwise poorly absorbed into cells—to enter in high concentrations.

This results in **targeted tumor destruction** with **minimal systemic toxicity**, given that the electric pulses are applied locally and the chemotherapeutic doses used are significantly lower than in conventional systemic regimens.

ECT is:

- Highly selective (only electroporated cells are affected)
- **Repeatable and combinable** with other therapies (e.g., immunotherapy, radiotherapy)
- **Guideline-endorsed**: The **ESOPE project** (2006, updated 2018) established standard protocols that are now widely adopted across Europe.

## 2. IPO Lisboa: 16 Years, 1000+ Patients – A Benchmark in Southern Europe

The IPO Lisboa began its ECT program in 2008, incorporating the technique into clinical practice based on ESOPE guidelines and adapted protocols. The center has since treated **over 1000 patients** with a wide variety of tumor types and clinical indications.

Key milestones of this program:

- Consistent use of **validated procedures** (Cliniporator™ platform and since 2018 Epore™ platform)
- Close collaboration across disciplines: surgical, medical, dermatological, and palliative oncology
- Standardization of patient selection criteria and treatment mapping
- Internal outcome monitoring and participation in multicenter European data registries ( Pioneer Registry)

IPO Lisboa's data has contributed to the validation of ECT for inclusion in clinical practice recommendations and comparative effectiveness studies.

## 3. Expanded Clinical Indications

## A. Basal Cell Carcinoma (BCC)

ECT has shown complete response (CR) rates of 80–90% in localized BCC, particularly:

- In cosmetically sensitive areas (e.g., periorbital, nasal, auricular)
- In frail or elderly patients where surgery or radiotherapy is contraindicated
- In multifocal or recurrent BCCs

Advantages:

- **Tissue preservation** (important in facial structures)
- Minimal scarring, with better cosmetic outcomes than surgical excision
- Outpatient feasibility, low need for anesthesia
- Low recurrence rates after complete response

Although ECT is not yet a first-line treatment in all guidelines, it is recognized in **European consensus documents** as a valid option for difficult or unresectable BCCs.

## **B.** Cutaneous Metastases of Malignant Melanoma

This is one of the most studied and validated applications of ECT. IPO Lisboa has treated hundreds of melanoma patients with cutaneous or subcutaneous metastases.

Published data (Campana et al., 2016; Sersa et al., 2008) show:

- Overall objective response (OR) rate: ~85%
  - **Complete responses**: 50–60%
  - Partial responses: 25–35%

IPO Lisboa data are consistent with these figures.

Benefits include:

- Local control in previously treated or inoperable lesions
- Fast symptom relief (pain, bleeding, ulceration)
- **Immunogenic potential**, possibly enhancing systemic responses when combined with checkpoint inhibitors (ongoing trials)

ECT is now included in the **ESOPE recommendations for melanoma skin metastases**, and referenced in **national clinical guidelines** in several European countries, even in EADO guidelines and from a few months in ESMO guidelines for locoregional disease in paleative and local control setting.

## C. Cutaneous Metastases of Breast Cancer

A common and distressing late manifestation in breast cancer is chest wall cutaneous recurrence. These lesions often resist to systemic treatments and severely impair quality of life.

IPO Lisboa has treated dozens of these patients with significant benefits:

- OR rates: 70–80%, including CR in >40% even in patients in end-line treatments after failure of all systemic and local options of treatment.
- Rapid reduction of symptoms such as:
- Bleeding and exudate
- Pain and malodor
- Functional impairment

ECT in this context:

- Can delay, avoid or potenciate further systemic therapy
- Is safely repeatable

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• Can be applied even in previously irradiated fields

Recognized by **ESOPE guidelines** and increasingly adopted in **palliative care protocols** across Europe.

## D. Kaposi's Sarcoma (HIV-Negative)

Kaposi's Sarcoma (KS), although rarer in immunocompetent patients, has been successfully managed with ECT at IPO Lisboa in HIV-negative individuals.

Clinical results:

- CR rates up to 95% in localized lesions
- Excellent cosmetic results
- No systemic side effects observed

ECT provides a useful alternative to radiotherapy or systemic chemotherapy, especially when:

- Lesions are localized and symptomatic
- The patient is reluctant or unable to undergo systemic treatment

Despite limited large-scale studies, case series (including IPO Lisboa's published internal data) support ECT as a viable, safe local treatment for classic or endemic KS.

## 4. Advantages and Clinical Impact

Across all tumor types, ECT offers:

- **High response rates** (typically 70–90% depending on histology and lesion type)
- Excellent safety profile (few Grade ≥2 adverse events)
- Outpatient or short-stay procedure
- Short treatment time (~30–60 minutes)
- Preservation of surrounding structures (nerves, vessels, skin integrity)
- **Positive patient-reported outcomes**: high satisfaction, low burden

These features make ECT especially suitable for:

- Frail, elderly or polymorbid patients
- Previously treated or irradiated areas
- Palliative scenarios where maintaining quality of life is key

## 5. Emerging Applications in Solid Tumors

IPO Lisboa is involved in exploratory use of ECT for **deep-seated tumors**, in collaboration with surgical oncology and interventional radiology:

- Hepatic metastases via laparoscopic or open intraoperative access
- Pancreatic and adrenal tumors (in development)
- Rectal e esophageal tumors (Endoscopic approach)
- Combination with systemic therapies, including immunotherapy

Early clinical data (Edhemovic et al., 2014) suggests:

- Tumor control in selected liver lesions
- Feasibility with minimal complications
- Immunogenic cell death mechanisms being investigated

These developments, though experimental, indicate that ECT may evolve into a **core technique** for **multi-modal treatment strategies**.

## 6. From Human to Veterinary Oncology – A Translational Perspective

The experience accumulated at IPO Lisboa and other centers serves as a powerful model for veterinary applications of ECT. Key shared principles include:

- Need for local, repeatable, well-tolerated cancer treatments
- Benefit of preserving function and appearance (e.g., limbs, face, perineal areas)
- Possibility of combining ECT with systemic therapies (in veterinary oncology, e.g., NSAIDs, TKIs)

Collaborative efforts across species can:

- Validate mechanisms of action in immunocompetent models
- Optimize device use and pulse parameters
- Improve quality of care for companion animals

ECT is thus a unique platform for **comparative oncology**, linking innovation in human hospitals to frontline veterinary practice.

### Electrochemotherapy and Immunotherapy: Mechanisms, Immunogenic Potential, and Emerging Combinations in Human and Veterinary Oncology

## Maja Čemažar, Ph.D.

Electrochemotherapy (ECT) is a local ablative therapy that combines electroporation with chemotherapeutic agents enhancing drug uptake and cytotoxicity in tumor cells. In the clinical practice, bleomycin and cisplatin are predominantly used, but other agent such as calcium electroporation also reached clinical trials. In preclinical level, studies focusing on the use of oxaliplatin are also underway. Initially, ECT was developed for cutaneous and subcutaneous tumors of various malignancies, but is now used also for deep seated tumors, such as tumors in liver and for bone metastases. The mechanisms of antitumor effectiveness of ECT are multifaced and include (a) direct cytotoxic effect due to the increased delivery of cytotoxic drugs to the cells, (b) antiangiogenic effect by the action on tumor blood vessels causing vasoconstriction and death of tumor endothelial cells and (c) immune modulation. Specifically, ECT induces immunogenic cell death (ICD), triggering an immune response through the release of damage-associated molecular patterns (DAMPs) and potentially tumor neoantigens. Preclinical and clinical studies indicate that ECT is more effective in more immunogenic tumors and that ECT can act as in situ vaccination. In situ vaccination is defined as a therapy which exploits tumor associated antigens (TAAs) in the vicinity of the tumor to induce a TAA specific systemic adaptive immune response. Therefore, several preclinical and also clinical trials have been performed to evaluate the combination of ECT with different types of immunotherapies. In preclinical studies in different tumor types, it was shown that either immunotherapy with IL-12 or immune check point inhibitors contributes more to antitumor effect produced by ECT in less immunogenic tumors. In veterinary oncology, the combination of ECT and gene electrotransfer of plasmid encoding IL-12 was evaluated in companion dogs with mast cell tumors. We demonstrated that the combined approach where both treatment ECT and gene electrotransfer of plasmid encoding IL-12 were administrated intratumorally in the same session were significantly more effective compared to ECT alone or when gene electrotransfer was performed peritumorally.

In human oncology, ECT is currently used in more 180 centers across Europe, mainly for cutaneous and subcutaneous tumors. ECT was first combined with immunotherapy ie. immune check point inhibitors in the treatment of melanoma cutaneous nodules. Currently, 10 studies, also on breast cancer, hepatocellular carcinoma and squamous cell carcinoma, reported the combined use of ECT with immune check point inhibitors, all reporting beneficial role of the combined treatment. In veterinary oncology, a PD-L1 inhibitor (gilvetmab) has recently become available, offering new opportunities for immunotherapy in animals. However, further studies, also at the preclinical level, still need to elucidate the underlying mechanisms of the combined treatment in tumors with different tumor microenvironment, to find the best protocols for combination and to determine to biomarkers for selections of the patients that would benefit from the combination.

## Electrochemotherapy in Veterinary Oncology: Practical Applications and Treatment Optimization

## Nataša Tozon

Electrochemotherapy (ECT) is a relatively new localized treatment modality in both human and veterinary oncology to manage solid tumours of various histology. The safety and efficacy of the treatment was demonstrated in different animal species.

Electrochemotherapy utilizes electroporation as a process where electric pulses transiently permeabilize cell membranes to augment the intracellular accumulation of chemotherapeutic drugs, such as bleomycin and cisplatin, thereby enhancing their antitumor efficacy.

Although the success of therapy varies depending on the type of tumour, considerable differences can be observed even within the same histological tumour types:

A good knowledge of biomarkers, such as histologic tumour type, is an indispensable tool for tailoring treatment regimens and predicting local and systemic response to treatment.

Therefore, it is important to identify other types of biomarkers that could serve as predictive factors for treatment success to contribute to the increasing recognition of ECT for tumour treatment in veterinary oncology.

The first report on the use of ECT in veterinary medicine dates to 1997 (Mir L, 1997). In 2001, our group published the first paper on the safety and efficacy of ECT for the treatment of canine and feline tumours (Tozon N, 2001). To date, the number of publications has grown to over 100. In 2016, a first operation procedure on the use of ECT was published (Tozon, 2016), which includes all the important details of the successful application of the method and has remained practically unchanged to this day. Nevertheless, years of experience have led to additional findings. Firstly, the therapy has proven to be more successful in smaller tumours up to 2 cm in diameter, and based on the pharmacokinetics of bleomycin, we now know that the optimal time for application of electric pulses is between 8 and 28 minutes after intravenous administration of the cytostatic drug, and we also know that the process of tumour necrosis is completed mostly in 4 to 6 weeks after treatment. We also know that the therapy is completely safe, that it provides long-term local control of the disease and that it can improve the local control after surgical resection, when safety margins cannot be achieved. One of the advantages of ECT is its potential to deliver effective results after a single treatment. However, in cases of partial response or tumour recurrence, the procedure can be safely repeated, often with equal or improved efficacy.

The clinical studies have shown that the expected objective response (OR) depends on the type of tumour: epithelial tumours (perianal adenomas and adenocarcinomas) respond in 100%, round cell tumours (MCT) in 85%, mesenchymal tumours (STS) in 75% and oral tumours (oral melanoma (OM), oral SCC) in 40%. The OR in ECT as adjuvant therapy for unclean margins can be expected to be 90% for both STS and MCT. The OR also decreases with advancing clinical stage.

In summary, ECT has established itself as a safe and effective treatment option for various cutaneous and subcutaneous tumours in veterinary patients, offering a viable alternative or adjunct to traditional surgical interventions, ensure the long-lasting local control of the disease with minimal said effects, excellent functional and cosmetic effects.

Despite the simplicity of ECT, appropriate use in clinical practice requires knowledge of the mechanisms of action, which are crucial for the success of the treatment and the avoidance of possible side effects.

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#### **Electroporation-Based Therapies in non-cutaneous tumours**

Matías Tellado VetOncologia, Buenos Aires, Argentina

Electrochemotherapy (ECT) is widely used in veterinary medicine for the local control of small, superficial cutaneous tumors. However, its indications can be broadened through combination with surgery in selected non-cutaneous tumors, particularly in settings where radiotherapy is unavailable. ECT involves the delivery of electric pulses to tissues after administration of an antineoplastic agent, typically bleomycin or cisplatin. Since electroporation is a physical phenomenon, drug uptake is independent of tumor histology, allowing ECT to achieve consistently high objective response rates across diverse tumor types in dogs, cats, horses, and humans.

Three notable non-cutaneous applications of ECT include the treatment of oral tumors, nasal tumors, and feline injection-site sarcomas (FISS).

In oral tumors, ECT has been primarily used for palliative purposes. In early-stage oral malignant melanoma, ECT can achieve high response rates and prolong survival. However, in advanced stages (III–IV), survival tends to decline due to factors such as tumor size, invasiveness, and metastatic progression. In these cases, combining ECT with surgical resection improves local control, extends survival, and provides more rapid symptom relief compared to ECT alone. Intraoperative application of ECT to surgical margins—both lateral and deep— has to be performed carefully and thoroughly. ECT can effectively treat areas with incomplete excision, helping preserve healthy tissues and improve both recovery and overall outcomes.

For nasal tumors, while ECT alone has demonstrated high efficacy in treating feline nasal planum squamous cell carcinoma, results in dogs are more variable due to deeper structural invasion. In dogs, surgical resection followed by ECT on inadequate margins yields better outcomes. Additionally, for intranasal tumors, the use of intracavitary electrodes such as SiNE® and Nasal-Cath® enables palliative treatments either as standalone therapies or combined with surgery, particularly when radiotherapy is unavailable or declined. Pre-treatment CT imaging is critical to evaluate tumor extent and guide the optimal therapeutic strategy.

Regarding FISS, the current gold standard remains wide surgical excision, often necessitating aggressive approaches such as limb amputation or extensive abdominal or thoracic wall resection. When surgical margins are compromised, adjunctive megavoltage radiotherapy significantly improves outcomes. In the absence of radiotherapy, combining surgery with intraoperative ECT offers a viable alternative to extend both disease-free and overall survival. However, ECT as a standalone therapy is discouraged for large, infiltrative lesions; it yields superior results when applied during surgery, especially in suboptimal surgical planning scenarios.
# Electrochemotherapy WORKSHOP in Small Animal Oncology: Practical Applications in Canine and Feline Patients

# Summary

This dry lab workshop offers a hands-on and clinically oriented introduction to electrochemotherapy (ECT) in small animal oncology. Divided into canine and feline modules, the workshop covers device setup, therapeutic indications, and real-life applications using simulation models. Participants will rotate between two dedicated rooms — one focused on canine cases and the other on feline — engaging in both theoretical content and practical demonstrations using simulation models. This session is ideal for veterinary oncologists looking to incorporate ECT into practice with confidence and a solid foundation.

# Date & Time

Saturday, May 24th, 2025 Time: 14:20 – 18:00 Location: Dry Lab – Room A & Room B Participants: Max. 40 (divided into two groups of 20, rotating rooms) Schedule:

Time	<b>Room A – Canine Group</b> Facilitator: Matias Tellado	<b>Room B – Feline Group</b> Facilitator: Natasa Tozon
14:20 – 16:00	Canine ECT: Devices, Clinical Use & Practical Training	Feline ECT: Devices, Clinical Use & Practical Training
16:00 – 16:20	Break (all participants)	Break (all participants)
16:20 – 18:00	Group 2 rotates to Room A Repeated session with new group	Group 1 rotates to Room B Repeated session with new group

## **Learning Objectives**

- Understand the mechanism and clinical rationale of electrochemotherapy
- Review available devices and electrode types used in ECT
- Identify common tumor types and anatomical locations treated with ECT in dogs and cats
- Practice electrode handling and ECT protocol application on simulation models
- Learn from experienced ECT clinicians and discuss clinical decision-making

# Exploring opportunities for client support mechanisms through pain clinics and the ever-changing world of artificial intelligence

# Ana Carina Costa

PgCertAVN Anaesthesia and Analgesia, NCert(Anaesth), NCert(PhysioTech), Anaesthesia and Pain Clinic RVN

# Learning Objectives

- Understand the role of pain clinics in palliative care and their impact on the cancer patient's quality of life.
- Identify signs and behaviours indicative of pain in veterinary oncology patients.
- Develop care plans that assist owners in recognizing signs of pain, using pain scoring scales, and accommodating environmental changes.
- Incorporate AI tools in pain assessment and activity tracking, understanding their benefits and limitations

# Introduction

Pain management is a fundamental aspect of veterinary oncology, as it significantly influences the quality of life (QOL) of cancer patients. The role of pain clinics in assessing, managing, and supporting both the animal and the owner through the palliative care journey is pivotal. Pain clinics provide a collaborative environment where veterinary nurses work alongside veterinarians, oncologists, and physiotherapists to offer both emotional and practical support to owners. This lecture will explore the role of pain clinics in veterinary oncology, focusing on the nurse's perspective, the impact of artificial intelligence (AI) tools in pain management, and the importance of a multidisciplinary approach in supporting owners through the pain management process.

## The Role of Pain Clinics in Veterinary Oncology

Pain clinics are a critical part of the palliative care team, offering a multi-disciplinary approach to pain management in cancer patients. Nurses are integral to the clinic's function, providing ongoing assessment, administering treatments, and educating owners on pain management strategies (Paz et al., 2024). In addition, nurses ensure that patients' comfort and well-being remain central, working with veterinary oncologists and pain specialists to create individualized care plans that address both pain relief and the overall treatment goals of the patient (Biller et al., 2016). Regular follow-ups in pain clinics allow for the adjustment of pain relief therapies as needed, ensuring that each patient's pain is effectively managed.

# **Recognizing Pain in Cancer Patients**

Identifying signs of pain in veterinary oncology patients can be particularly challenging due to the varied ways animals express discomfort. Common indicators include changes in appetite, posture, mobility, and vocalization (Rancilio et al., 2015). Pain may also manifest in more subtle behaviours, such as decreased activity, self-isolation, or changes in grooming habits (Paz et al., 2024). Validated pain scoring scales and QOL questionnaires, are useful tools in assessing pain at home and evaluating the patient's overall well-being. Educating pet owners on the use of these pain scoring scales is a vital aspect of the nurse's role. Empowering owners to identify signs of pain allows them to actively participate in their pet's care and ensures more accurate pain management decisions.

# Challenges in Pain Scoring and the Role of AI Tools

Pain scoring is often challenging for owners, many of whom may struggle to accurately

assess and score their pet's pain. Recent advances in AI technologies offer potential solutions for this issue. AI algorithms that assess pain through behavioural and physiological data have been tested, and they could soon play a significant role in managing cancer pain. AI-based systems, such as those discussed by Steagall et al. (2023), use deep learning models to predict pain in animals, including applications like the Feline Grimace Scale. These technologies can enhance pain management by offering more accurate, real-time assessments. Technologies like activity trackers, which provide objective data on a patient's activity and rest patterns, are already being used to monitor how pain may affect a patient's routine and level of activity (Chiavaccini et al., 2024).

# The Role of the Multidisciplinary Team

A multidisciplinary approach to pain management is essential for the comprehensive care of oncology patients. As described by Paz et al. (2024), a pain clinic fosters collaboration among veterinary nurses, oncologists, and physiotherapists, which improves the overall patient care experience. This approach not only ensures better management of pain but also provides owners with the emotional and practical support they need during the palliative care journey. The use of AI tools in pain management can support this team approach by providing more objective assessments, which can be used to adjust treatments and ensure that the pain management plan is tailored to the individual needs of the patient.

# Conclusion

In veterinary oncology, pain management is a critical component of ensuring the quality of life for cancer patients. Pain clinics, with their multidisciplinary teams, play a key role in supporting both the patient and the owner throughout the palliative care process. The integration of AI technologies for pain recognition and scoring offers exciting possibilities for improving pain management, allowing for more accurate and timely interventions. Nurses play a central role in educating owners, assessing pain, and managing therapies, and their work is essential to optimizing care for cancer patients in veterinary oncology.

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## ECT – Principles, Application, Case Studies

## Matías Tellado VetOncologia, Buenos Aires, Argentina

#### **General considerations**

Electrochemotherapy (ECT) is a highly effective treatment modality in oncology for local control of the disease. In the past decade, we've seen significant advancements in the development of devices and electrodes, encouraging veterinary oncologists worldwide to adopt this therapy as a treatment option. ECT works by exposing tissue to an intense and specific electric field that creates pores in the cell membrane. These pores are temporary, and cellular viability is preserved, a process known as reversible electroporation. This phenomenon increases drug uptake considerably, regardless of tumor histology, increasing its therapeutic effect, in a therapy called ECT. Only two drugs have been consistently demonstrated to produce high response rtes, bleomycin and cisplatin



A. The antineoplastic agent, typically bleomycin, which is impermeable to the cell membrane, is injected. B. After 5-8 minutes to ensure proper distribution of the agent, the electric field is applied, inducing the formation of reversible pores in the cell membrane that allow the agent to enter the cell. C. The pores seal, leaving the membrane intact and the cell viable with bleomycin inside. From this point on, during replication, the cell will undergo the process of mitotic death.

## Electrical parameters for effective electrochemotherapy

The electrical parameters for effective ECT had been precisely established in many scientific publications, such us the European Standard Operating Procedures for Electrochemotherapy (2016), and the Veterinary Guidelines for Electrochemotherapy of Superficial Tumors (2021). They are 8 monopolar square-wave 100µs long pulses of 1,000 V/cm at 1 to 5,000 Hz. This field must be delivered consistently in the tumor and margins. Adequate delivery largely depends on the correct technique, the design and geometry of the electrodes, and on the capacity of the electroporator to sustain the voltage steady throughout the pulses. Most veterinary devices are self-configurable, however, when using manual devices, it is essential to correctly set it according to the electrode used.

Most used electrodes include plates for superficial treatments and needles for tumors that invade deeper. There are different designs of needle-electrodes which differ in the number of needles, their diameter, material, and spacing. Understanding these differences is fundamental to choosing the best electrode for each case.

Key aspects for a successful ECT include adequate device configuration (for manual devices), selecting the right electrode for each patient, selecting the adequate administration route of the drug (local for small tumors and i.v. for the rest), precise and careful technique, and finally the use of disposable electrodes (as they provide adequate sharpness and electrical conduction in each treatment).

# **Patient selection**

The use of ECT as part of a treatment strategy should focus on achieving local disease control when surgery is not feasible or accepted by the owner. In these cases ECT can be an option in combination with surgery, or as stand-alone therapy. It is well known that non-oncological surgery—where resection margins are narrow or incomplete—often leads to high local recurrence rates, allowing the disease to progress to regional lymph nodes or even metastasize.

In this context, ECT may be indicated as:

- A single therapy for small tumors without any other interventions (e.g., squamous cell carcinoma of the nasal planum in cats).
- Intraoperatively, applied in the surgical bed for neoplasms resected with insufficient margins.
- As a neoadjuvant therapy to reduce tumor burden and make surgery feasible (e.g. perianal tumors).
- As adjuvant therapy on scars to reduce local recurrence rates and extend diseasefree survival (e.g., soft tissue sarcomas).

# Step-by-step procedure

- **Tumor area:** Prepare the treatment area similarly to how you would do for surgery.
- Anesthetic procedure: Administer general anesthesia, combined with local or regional anesthesia as needed based on the treatment area. The pain management plan should match what would be used in a surgery of that area.
- Choice of the drug and way of administration: I.v. Bleomycin is the recommended drug and way of administration for virtually all cases. The dose is 15,000 IU/m<sup>2</sup> in bolus over 30-45 seconds.
- **Drug distribution:** After the administration, wait 8 minutes for optimal distribution (can be 5 minutes in small animals).
- **Application of pulses:** Ensure that the entire tumor volume and its safety margin are covered. Ideally, treatment can continue for up to 45 minutes after the drug has been distributed. If this time is exceeded, do not stop the treatment, continue until finishing, but perform a close follow-up of the lesions treated outside the optimal treatment window.
- **Recovery:** Monitor post-anesthetic recovery, provide analgesia, and prophylactic antibiotics as needed.
- **Follow-up:** Schedule weekly controls through photographs, and monthly in-person evaluations to assess the response, and determine if another ECT session is needed.



# Technical aspects during the procedure

During treatment, it's important to focus on ensuring only a slight overlap of the electrode in the treated area. This overlap should be enough to make sure that no areas are left untreated, but not so much that it becomes excessive. Too much overlap can lead to irreversible electroporation and unwanted tissue necrosis. While this isn't usually an issue in tumor tissue, it definitely is in healthy tissue.



• For rounded lesions that protrude, always position the electrode **perpendicular to the surface where the tumor sits**, and not to the tumor's surface. The latter could cause too much overlap in the core of the tumor producing unneeded necrosis and is not adequately for treating the base of the lesion.



 If you are treating hard, fibrous lesions, the needles might bend – either separating or coming together. If they separate, the electric field could end up being insufficient. If they come too close, it increases the risk of producing an electric arch between the needles. It is important to insert the needles carefully into dense masses and check that they haven't deviated from their intended path to ensure an effective treatment. If an arch is produced (the device will show it on the screen) remove the electrode, correct needle alignment and treat the same area again, as the arch does not provide an adequate electric field.



- When it comes to areas involving teeth, if a tooth is loose, it is better to remove it and treat the entire dental socket.
- Plate electrodes generate an effective electric field primarily at the surface, extending no more than 3 mm in depth. It is recommended to use a water-based conductive gel between the electrode and the tissue to improve contact. It is important to note that treatment depth cannot be compensated by applying the electric pulses repeatedly at the same spot. If you need more depth of treatment use needle electrodes.
- Needle electrodes can provide an effective electric field only between the needles. The use of gel with this electrode is optional. Using a disposable electrode for each patient provides adequate electrical conduction and adequate sharpness.

# **Contraindications for ECT**

While ECT does not rule out other treatments, there are certain cases where a clinical oncologist should consider carefully whether to recommend or not ECT.

- **Pregnant females:** Bleomycin and cisplatin can be potentially harmful to the fetus. Electroporation with intratumoral administration of calcium is an option, but the anesthetic risks need to be considered.
- Lactating females: Early weaning is recommended.
- Males and females with high genetic value: In these cases, it's generally best to avoid bleomycin and cisplatin. The risks related to fertility are low but still present.
- Animals destined for human consumption: ECT is not recommended. Electroporation with calcium can be an option.
- **Patients with high tumor burden:** Those with advanced local stages typically have poor chances of local disease control with ECT alone. In these situations, it's better to consider ECT in combination with surgery.
- Late-stage tongue cancer and late-stage canine nasal neoplasms: These areas can be quite sensitive to ECT. The risk of lingual necrosis or severe tissue damage should be weighed carefully by the treating oncologist and alternative treatment options should be considered. In contrast, nasal neoplasms in cats usually show minimal side-effects when using fine-needle electrodes.
- Patients with renal failure: While ECT is not contraindicated, caution is advised

# Response to ECT:

- **Typical response:** You can usually expect to see maximum reduction or the complete disappearance of the treated lesion within 4-6 weeks after the procedure.
- **Recurrence and regrowth:** If the lesion starts to grow again after treatment, that indicates a recurrence, and a new session should be scheduled as soon as possible. It is not recommended to perform ECT in a fixed time basis, as responding tumors will not benefit from additional treatment.
- Apparent absence of response: If the lesion does not change in size or grows, probably the cells are not replicating. It is advisable to consider alternative treatment options.



# Potential Complications Associated with Electrochemotherapy (ECT)

- Edema in specific areas: Edema can be significant following treatment and poses a particular risk in patients with tumors located in the pharynx or larynx, potentially leading to airway obstruction. Careful evaluation of the airway is critical before, during, and after the procedure, especially regarding risks during intubation and extubation.
- **Tachypnea:** Reflex tachypnea may occur after the delivery of each pulse train. This reaction can be minimized by incorporating muscle relaxants into the anesthetic protocol. It is important to recognize that this reflex does not indicate pain or inadequate anesthetic depth.
- **Tachycardia and pain:** Depending on tumor location, the procedure can induce significant pain. It is essential to adjust analgesic management accordingly. The use of local or regional anesthesia not only improves pain control but also reduces the need for systemic anesthetics, resulting in smoother recoveries and faster resumption of food and water intake post-procedure.
- **Pseudo-obliteration of the nostrils:** When ECT is applied to areas involving both nostrils, close monitoring during anesthetic recovery is crucial. Post-treatment swelling and inflammation can compromise the airway, necessitating proactive airway management.
- **Necrosis:** Mild, localized necrosis can occur after ECT without negatively impacting wound healing or quality of life. However, extensive necrosis, wound dehiscence, or significant deterioration in quality of life may result from technical errors, such as excessive overlap of treated areas. Proper technique and adequate superimposition are key to minimizing these risks.
- **Rapid recurrence:** Tumor recurrence may occur more frequently when large tumors are treated, when inappropriate electrodes are used, or when improper electrode positioning leaves untreated areas. Recurrence is also associated with inadequate electric field strength, often due to insufficient device power or electrode reuse.

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# Chemo's Gut Check: Keeping the GI Tract in the Game

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Chemotherapy, a cornerstone in cancer treatment, is designed to eradicate malignant cells by targeting their rapid division. However, this non-selective targeting means that normal cells with high turnover rates, such as those in the gastrointestinal (GI) tract, are also affected. Consequently, patients undergoing chemotherapy often experience significant GI side effects, which can severely impact their quality of life. This presentation emphasizes the importance of preventive measures and owner education, as they are essential for minimizing discomfort and ensuring successful treatment outcomes.

# **MECHANISMS OF GI EFFECTS**

Chemotherapy drugs work by interfering with various stages of the cell cycle, such as DNA synthesis, cell division, and protein synthesis. This disruption prevents cancer cells from proliferating and spreading. However, these same processes in normal cells, particularly those lining the GI tract, are also disrupted, leading to side effects. The most rapidly increasing compartment of the GI tract is the cells lining the crypts. In healthy animals, the crypt cells from below replace epithelial cells along the villi. When crypt cells are damaged from chemotherapy, no replacement cells are available, resulting in delayed GI toxicosis manifesting as nausea, hyporexia, vomiting, and diarrhea 2 to 5 days post-treatment.

The damage to the GI tract by chemotherapy drugs primarily affects the rapidly dividing cells of the stomach and intestinal lining, leading to various symptoms. The severity of these symptoms can vary depending on the specific chemotherapeutic agent used, the dose, and individual patient factors. However, with the right management strategies, these symptoms can be alleviated. Chemotherapy-induced nausea and vomiting (CINV) are particularly debilitating, but with effective management, the patient's comfort can be significantly improved.

# COMMON GI SIDE EFFECTS Nausea and Vomiting (CINV)

Chemotherapy-induced nausea and vomiting (CINV) can significantly affect a patient's quality of life. These symptoms are caused by the activation of receptors in the digestive tract and brain, leading to nausea and the vomiting reflex. Acute CINV typically occurs within the first 24 hours post-treatment, while delayed CINV can occur 2-5 days later. Effective management of CINV is crucial to maintaining the patient's nutritional status and overall well-being.

Acute vomiting is often triggered by the rapid administration of chemotherapy drugs or those with high emetic potential, such as cisplatin, doxorubicin, dacarbazine, and streptozotocin. The mechanism involves releasing neurotransmitters and activating receptors in the chemoreceptor trigger zone (CTZ) and the brain's vomiting center. Proper dilution ratios and administration rates can reduce the number of acute vomiting episodes. Delayed vomiting, more common in veterinary patients, is typically due to direct damage to the rapidly dividing GI tract cells or centrally mediated CRTZ stimulation through gut vagal efferents. Drugs such as doxorubicin and vinca alkaloids commonly cause delayed vomiting, which manifests 2-5 days post-treatment.

Anticipatory vomiting, although common in human patients, is rare in veterinary patients. This type of vomiting is a conditioned response to stimuli associated with chemotherapy, such as smells, sights, and sounds of the treatment room.

# Diarrhea

Chemotherapy can cause both acute and chronic diarrhea. A sudden onset characterizes acute diarrhea and is often due to damage to the intestinal lining or an imbalance in gut flora. Chronic diarrhea results from persistent damage or inflammation within the gut. This can lead to severe dehydration and electrolyte imbalances, further complicating the patient's condition. Diarrhea can be particularly severe with drugs like toceranib phosphate, which increases intestinal permeability, leading to fluid and electrolyte leakage. Carboplatin is also associated with diarrhea due to its damaging effects on the intestinal lining and alteration of gut microbiota. This leads to inflammation and increased secretion of fluids into the gut, contributing to diarrhea. Managing diarrhea involves using medications like metronidazole, probiotics, and dietary adjustments to restore gut flora balance and ensure adequate hydration.

# Mucositis

Ulceration of the GI tract lining, known as mucositis, can occur, leading to pain and discomfort. This condition can affect any part of the GI tract and is often more severe with specific chemotherapeutic agents. Mucositis can significantly impair a patient's ability to eat and drink, leading to nutritional deficits and weight loss.

Chemotherapy-induced mucositis occurs because of the damage to the rapidly dividing epithelial cells lining the GI tract. When these cells are destroyed, the mucosal barrier is compromised, leading to inflammation, ulceration, and an increased risk of infection. This can be particularly challenging to manage, as it requires a combination of pain management, nutritional support, and possibly antibiotics to prevent secondary infections.

# **Anorexia and Weight Loss**

Chemotherapy can reduce the patient's appetite and subsequent weight loss, further complicating the patient's nutritional status and overall well-being. This can be particularly challenging in veterinary patients, as maintaining a good nutritional status is critical for their recovery and response to treatment.

Anorexia in chemotherapy patients can be caused by several factors, including nausea, vomiting, mucositis, and the overall stress of the treatment process. Appetite stimulants such as capromorelin, mirtazapine, and prednisolone can be used to help increase food intake. Capromorelin works by mimicking the hunger hormone ghrelin, binding to receptors in the hypothalamus and causing the sensation of hunger. Mirtazapine and prednisolone can also stimulate appetite, but their use needs to be carefully managed to avoid side effects.

# **Specific Chemotherapeutic Agents and Their GI Effects**

Different chemotherapeutic agents impact the GI tract in varying degrees. Understanding these effects is crucial for implementing appropriate management strategies.

- **Doxorubicin**: Known for causing acute vomiting and diarrhea, doxorubicin induces GI tract inflammation and irritation, releasing inflammatory mediators that trigger the vomiting center in the brain. Rapid administration of doxorubicin has also been associated with acute vomiting. Damage to the chemoreceptor trigger zone (CTZ) by doxorubicin can make animals more sensitive to the emetic effects of chemotherapy.
- Vincristine and Vinblastine: These agents affect the CTZ and cause gastrointestinal irritation and inflammation. This results in increased gastric acid secretion and changes in GI motility, leading to nausea and vomiting. Despite their similarities, vincristine tends to cause more severe GI effects compared to vinblastine. Both drugs can also lead to ileus, a condition characterized by a lack of movement in the intestines, causing blockage and severe discomfort.
- **Carboplatin**: Associated with diarrhea due to its damaging effects on the intestinal lining and alteration of gut microbiota. This leads to inflammation and increased

secretion of fluids into the gut, contributing to diarrhea. Carboplatin can also cause delayed vomiting by damaging the crypt cells of the intestines, leading to prolonged recovery periods.

• **Toceranib Phosphate**: Notable for causing diarrhea by increasing intestinal permeability and causing fluid and electrolyte leakage. This drug can also lead to chronic diarrhea, which requires careful management and monitoring. Toceranib's impact on the GI tract can be severe, necessitating frequent monitoring and supportive care.

# MANAGEMENT AND PREVENTION OF GI SIDE EFFECTS

Effective management of chemotherapy-induced GI side effects is essential to improve patient outcomes and maintain their quality of life. Strategies include:

# Antiemetics

Drugs such as ondansetron, maropitant, and metoclopramide are commonly used to prevent and treat CINV. These drugs block receptors in the brain and digestive tract that mediate nausea and vomiting. For instance, maropitant is an NK1 receptor antagonist that inhibits substance P, making it practical for acute and delayed CINV. Ondansetron, a 5-HT3 receptor antagonist, is effective in preventing acute vomiting caused by high-emetic potential drugs like cisplatin and doxorubicin. Metoclopramide, with its prokinetic properties, is particularly useful for managing delayed CINV associated with medications like vincristine.

# **Proton Pump Inhibitors and Mucosal Protectants**

Medications like omeprazole and sucralfate help reduce inflammation and protect the GI lining from further damage. Omeprazole, a proton pump inhibitor, reduces acid secretion, while sucralfate forms a protective layer over ulcers, preventing further injury. These medications are essential in managing chemotherapy-induced mucositis and preventing the progression of ulcers.

## **Probiotics and Antibiotics**

Probiotics can help restore gut flora balance, and antibiotics like metronidazole are used to manage diarrhea caused by chemotherapy. Metronidazole has antibacterial, antiprotozoal, and anti-inflammatory properties, effectively treating acute and chronic diarrhea. Probiotics such as Lactobacillus and Bifidobacterium can help maintain a healthy gut microbiome, reducing the severity of diarrhea and other GI symptoms.

## **Nutritional Support**

Maintaining adequate nutrition is crucial. In severe GI side effects, hospitalization and supportive care may be necessary, including IV fluids and nutritional support. Nutritional support includes offering bland diets, increasing fiber intake, and ensuring the patient remains hydrated. Feeding small, frequent meals of easily digestible food can help manage anorexia and prevent weight loss.

## **Preventive Measures**

Preventive measures include adjusting chemotherapy doses, pre-treating with antiemetics, and using supportive care to mitigate the onset of severe GI side effects. Owners should be educated on recognizing early signs of GI distress and seeking timely veterinary care. Implementing dose reductions or drug holidays for patients experiencing severe side effects can help manage their overall treatment plan more effectively.

## Hospitalization and Supportive Care

In severe cases, hospitalization may be required to provide intensive supportive care. This includes administering IV fluids to manage dehydration, providing pain relief for severe mucositis, and using antiemetics to control vomiting. Hospitalization allows for close monitoring of the patient's condition and timely intervention to prevent complications.

# **Owner Education and Communication**

It is crucial to educate pet owners about the potential GI side effects of chemotherapy and how to manage them at home. Providing written instructions on diet modifications, medication administration, and signs of severe GI distress can help owners feel more confident in managing their pet's condition. Regular communication between the veterinary team and pet owners ensures that any issues are promptly addressed, improving the overall treatment experience for both the pet and owner.

# Conclusion

Chemotherapy is a powerful tool in cancer treatment but comes with significant side effects due to its impact on rapidly dividing normal cells. Understanding the mechanisms behind these side effects and implementing appropriate management strategies is crucial for improving patient outcomes and maintaining their quality of life. By knowing which chemotherapeutics are more likely to cause specific GI effects, veterinarians can better prevent and manage these adverse reactions, ensuring more successful and tolerable treatments for their patients. Effective communication with pet owners about the potential side effects and the importance of adherence to treatment protocols is essential for the success of the therapy.

Chemotherapy-induced GI side effects can be managed effectively with pharmacological interventions, nutritional support, and preventive measures. The goal is to minimize discomfort and ensure patients can continue their treatment with minimal disruption. As veterinary oncology continues to evolve, ongoing research and advancements in supportive care will further enhance the management of chemotherapy-induced GI side effects, ultimately improving the quality of life for cancer patients.

Keywords: chemotherapy, gastrointestinal, nausea, oncology, side effects

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From Nadir to Danger: Understanding and Treating Chemotherapy-Induced Sepsis

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# INTRODUCTION

Chemotherapy is a standard treatment used within veterinary oncology. There are several chemotherapeutic agents used to treat a variety of different types of cancer. Despite their differing mechanisms of action, the goal of each is the same: kill cancer cells. While doing their job, there are some expected, although not common, side effects. These include GI disturbances, as well as hematologic changes like neutropenia. While cancer is not often thought of as an emergency, chemotherapy-induced sepsis is one of the rare occurrences. Sepsis is generally considered within the realm of critical care. While fundamentally the same, there are some particular differences in approach to the cancer patient. These differences extend to the treatment and expectations for recovery as well.

# CHEMOTHERAPY

# **Chemotherapy Basics**

Chemotherapeutics are not widely used in veterinary medicine. They are often reserved for specialty veterinary practices by trained oncology teams. Most veterinary technology programs spend about one lecture period on their use. Due to this, only a few technicians understand how these agents work. In straightforward terms, chemotherapy acts against rapidly dividing cells and kills them. The different drugs do this differently, and not all of them are understood. Cancers grow and spread by shutting down or bypassing the body's normal cellular patterns, and the cells reproduce unchecked. This is how chemotherapy works at the most basic level. Most chemotherapy, however, is not target or cancer-specific. Other cells within the body are also rapidly dividing simultaneously as cancer cells. The most common are those within the GI tract and white blood cells.

## Side Effects

Some of the most commonly known facts about chemotherapy are the side effects. In humans, as well as cats and dogs, anorexia, nausea, and immune suppression can be expected. These are more pronounced in humans because the doses are higher, and the outcome is remission. In veterinary medicine, the goals center around quality of life, so the doses are much lower, and the incidences of side effects are also lower. It is important to note that not all drugs affect animals the same way as human beings. A prime example is hair loss. This happens to most people undergoing chemotherapy treatment, but rarely in dogs and rarely in cats, except their whiskers. This is because human hair is most frequently in the growing phase when it can be affected by chemotherapy, leading to balding. This is also why it grows back after therapy is finished or discontinued. Animal fur is usually in the resting phase and is only affected when it is actively growing. This is why it can appear thin and is slow to grow back after shaving for diagnostics or catheter placement. The exceptions to this are those breeds that need grooming due to constantly increasing fur, like Bichons, sheepdogs, poodles, etc.

The previous side effects are also due to chemotherapy causing cell death among the rapidly dividing GI tract and bone marrow cells. When it comes to the GI tract, inflammation and damage generally occur 3-5 days after the administration of chemotherapy. This is why clients are often instructed to watch for anorexia, vomiting, or diarrhea during this time. It is often self-limiting and resolves by about 6-9 days post-administration. The anorexia is usually a sign of nausea and the precursor to vomiting. The sooner these can be addressed with anti-emetics and antidiarrheals, the better the experience will be for the pet and client.

# Neutropenia

Bone marrow suppression caused by chemotherapy affects more than just the white blood cells; the specific cell cycle of each cell type matters. Anemia is rarely caused by chemotherapy because red blood cells have a life span of 7-120 days. Chemotherapy affects the cells during reproduction, so only a tiny percentage of the red blood cell population is reproducing at one time. This is generally mild and only significant in the already anemic patient. Platelets are similar in their 5-10 day lifespan and are usually only affected by chronic chemotherapy. Granulocytes have the shortest lifespan, with neutrophils having a lifespan of 4-8 hours. This gives chemotherapy time to disrupt a majority of cell division and replication. Each chemotherapy drug has what is referred to as the nadir period. This is when the neutrophil count is expected to be at its lowest point post-administration. For many of them, this is 7-10 days after administration, but a few have longer nadirs of 10-14 days, and some even have delayed nadirs for 14-21 days. This is the ideal time for a CBC to be checked, but getting an accurate history from a client is also crucial. When the neutrophil count is below 1,000/µL, there is an increased chance of infection and sepsis.

# SEPSIS

# Definitions

Sepsis is defined as the systemic inflammatory response to infection. Common sites from which the bacteria originate in most septic cases are the GI tract, respiratory tract, severe dental disease, chronic urinary tract disease, and contaminated wounds. Severe sepsis includes the above but is also associated with organ dysfunction and hypoperfusion or hypotension. Septic shock adds a layer of hypotension that is refractory to volume expansion. All of these are due to the prolonged presence of bacteria within the bloodstream. All types of sepsis are medical emergencies. Treatment for the septic patient includes hospitalization and immediate corrective therapies and antibiotics. Extensive diagnostics are often needed to find the cause and determine the condition's full extent. Cancer patients differ, as the cause is usually known.

# **Predisposing factors**

Cancer offers multiple pre-disposing factors to sepsis. These include immune dysfunction caused by the cancer itself or treatment with corticosteroids, prevention of antibody production by splenectomy, malnutrition, prolonged hospitalization, and chemotherapy-induced. The most commonly studied and discussed is the chemotherapy-induced. How chemotherapy causes neutropenia and the resulting susceptibility to infection has already been discussed.

## Presentation

Chemotherapy-induced sepsis can look like many other issues in cancer patients. The timeline and history obtained by clients are critical. Signs in the patient can be vague and nonspecific: lethargy, weakness, inappetence, and febrile. It is important to note that the lack of a fever does not impact the severity of the disease, and the patient's overall health must be considered. The nadir period of the drug must be considered, and a CBC must always be performed. The absolute count of neutrophils is the most important, not the percentage of total white blood cell count.

Septic patients will generally present with tachycardia, brick-red mucous membranes (increased CRT), hypotension, altered mentation, and GI signs. At first, they can also have hyperglycemia followed by hypoglycemia. As it progresses to shock, the symptoms move to the other end of the spectrum with hypothermia, mm pallor, depression, and multi-organ failure. This can be avoided in the chemotherapy patient by strict adherence to follow-up exams and CBCs after any new chemotherapy treatment.

# **Treatment and Prevention**

As previously discussed, most septic patients require extensive and aggressive treatment. Oncologists have a chart they use as a guideline for the treatment of neutropenia following chemotherapy and possible sepsis:

## "Table 1"

The chemotherapy patient is at a higher risk for infection and sepsis if they are hospitalized. So, if they do not have a fever and are continuing to eat, it is best to send them home on oral antibiotics. The neutrophils have a rapid rebound rate and often increase 1-3 days after the nadir period. With this, the risk of infection is declining. Once a patient has experienced bone marrow suppression leading to neutropenia, the dose is altered to avoid it again. Prophylactic antibiotics are also often prescribed to be started along with the nadir period, usually 3-5 days after chemotherapy administration, through their next recheck and CBC appointment.

# CONCLUSION

While chemotherapy-induced sepsis is a form of sepsis at the basic level, it is handled very differently. This side effect is prepared for and not out of the blue, as other emergent conditions can be. There are prescribed protocols to follow, and the client can be ready for this worst-case scenario and plan ahead of time.

## Table 1

	Prophylaxis	Grade 2/Mild Toxicity	Grade 3/Mod Toxicity	Grade 4/Severe Toxicity
Neutropenia		1000/µL	500-999/µL	<500/µL
Broad-spectrum aerobic antibiotics	Not recommended	No	Oral Repeat CBC in 2-3 days Do not hospitalize	Oral IV if fever CBC in 24 hours
Broad-spectrum anaerobic antibiotics	No	No	No	Not routine unless refractory to aerobic antibiotics
Parenteral fluids (SQ or IV) and supportive care	No	No	Not routine unless febrile	Hospitalize if febrile

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# When Chemo Goes Rogue: Extravasation Survival Skills

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### Introduction

Extravasation, defined as the unintentional leakage of vesicant or irritant medications into surrounding tissues, represents a significant emergency during chemotherapeutic administration. Mismanagement can lead to severe tissue damage, delayed healing, infection, or even the need for surgical intervention.

This document outlines drug classifications, antidote availability and mechanisms, symptom timelines, common causes of extravasation, treatment protocols, and prevention strategies to equip veterinary professionals with essential survival skills.

### **How Extravasation Occurs**

Extravasation typically results from mechanical or patient-related factors, including:

- Poor vein selection (fragile, mobile, or compromised veins)
- Improper catheter placement or catheter dislodgement
- High infusion pressure or forceful administration
- Movement of the patient during infusion
- Fragile or compromised vasculature from prior therapies

Understanding these pathways is critical because even careful infusion practices cannot eliminate all risks. Prevention strategies must address mechanical, patient-related, and drug-specific vulnerabilities to reduce extravasation events truly.

# **Understanding the Risk: Drug Classifications**

Chemotherapeutic agents are classified based on their potential tissue impact upon extravasation.

- Neutrals
  - Neutrals are agents that, if extravasated, typically cause little or no tissue damage. They may result in mild local inflammation, but serious tissue injury is rare. Patients should be monitored for delayed symptoms, especially if large volumes infiltrate.
- Irritants
  - Irritants can cause pain, redness, and swelling at the infusion site but do not usually lead to necrosis or ulceration. The severity of symptoms often depends on the concentration and volume of the extravasated drug.
- Vesicants
  - Vesicants are agents that can cause severe tissue injury, including blistering, ulceration, and necrosis. Immediate action is required if these agents extravasate.
  - Vesicants are further divided into two groups:
    - DNA-binding vesicants: Bind to DNA and remain active within tissues, leading to ongoing and progressive tissue destruction if not treated.
    - Non-DNA-binding vesicants: Cause localized cellular injury, but the damage tends to be more contained and less progressive compared to DNA-binding agents.

The following chart summarizes chemotherapy drug classifications based on their behavior when extravasated:

Classification	Behavior When Extravasated	Example Drugs
Neutrals	Minimal tissue reaction; may cause	Bleomycin, Cyclophosphamide,
	mild inflammation	Cytarabine, L-asparaginase
Irritants	Cause pain, redness, inflammation;	Carboplatin, Dacarbazine,
	rarely cause necrosis	Mitoxantrone
Vesicants	Localized tissue injury; limited spread	Vincristine, Vinblastine,
(Non-DNA-binding)		Vinorelbine, Rabacfosadine
Vesicants	Progressive, worsening tissue	Doxorubicin, Mechlorethamine,
(DNA-binding)	damage	Actinomycin D

# **Recognizing Extravasation**

Recognizing an extravasation event early is critical to minimizing the extent of tissue injury. During chemotherapy infusion, the earliest signs may include swelling or puffiness at the catheter site, redness or blanching of the skin, pain, burning, or resistance during drug administration. Leaking at the catheter insertion point may also occur.

Symptom progression varies depending on the agent extravasated. The following chart illustrates the expected timelines:

Timeframe	Neutrals	Irritants	Vesicants Non-DNA-binding	Vesicants DNA-binding
0–2 hours	Usually no symptoms or mild swelling	Mild pain, erythema, swelling	Burning, redness, swelling	Severe burning pain, swelling, blanching
24–48 hours	Minor inflammation may peak, then resolve	Redness and discomfort peak; generally no tissue loss	Inflammation persists; possible superficial blistering	Worsening inflammation; blistering likely
3–7 days	Symptoms resolve	Full recovery expected unless large volume	Healing or superficial injury; rare necrosis	Ulceration, tissue necrosis becomes visible
1–2 weeks	Complete resolution	Full resolution expected	Full healing if treated appropriately	Progressive deep tissue injury if untreated

Because of these risks, any change in the infusion site appearance, catheter function, or patient comfort must be treated seriously and evaluated for possible extravasation. Early intervention dramatically improves outcomes, making recognition skills as critical as the management steps that follow.

## **Treatment Principles**

When extravasation is suspected, immediate action is critical. Stop the infusion without removing the catheter. Aspirate any residual drug without applying pressure, then remove the catheter carefully.

- DNA-binding vesicants: Apply cold compresses and administer antidotes like dexrazoxane or sodium thiosulfate.
- Non-DNA-binding vesicants: Apply warm compresses and consider hyaluronidase administration.
- Irritants and Neutrals: Apply cold compresses for comfort and monitor the site closely.

Documentation, reassessment, and escalation if necessary are essential components of management.

# **Drug-Specific Interventions**

Management strategies vary depending on the drug involved. The chart below outlines specific management strategies for common chemotherapy agents used in veterinary medicine:

Drug	Compress Type	Antidote/Intervention	Notes	
Neutrals	•	•	-	
Bleomycin	Cold compress	Supportive care	Minimal reaction expected	
	(optional)			
Cyclophosphamide	Cold compress	Supportive care	Minimal reaction expected	
	(optional)			
Cytarabine	Cold compress	Supportive care	Minimal reaction expected	
	(optional)			
L-asparaginase	Cold compress	Supportive care	Minimal reaction expected	
	(optional)			
Irritants				
Carboplatin	Cold compress	Supportive care	Monitor for inflammation	
Dacarbazine	Cold compress	Supportive care	Monitor closely	
Mitoxantrone	Cold compress	Supportive care; escalate if	Monitor closely	
		worsens		
Vesicants (Non-DNA-binding)				
Rabacfosadine	Warm compress	Supportive care	Disperse and dilute	
Vinblastine	Warm compress	Hyaluronidase (SQ)	Disperse and dilute	
Vincristine	Warm compress	Hyaluronidase (SQ)	Disperse and dilute	
Vinorelbine	Warm compress	Hyaluronidase (SQ)	Disperse and dilute	
Vesicants (DNA-binding)				
Actinomycin D	Cold compress	Supportive care	Localize and monitor for	
			necrosis	
Doxorubicin	Cold compress	Dexrazoxane (IV)	Start within 3 hours	
Mechlorethamine	Cold compress	Sodium thiosulfate (SQ)	Inject around site	

Chart 2: Drug-Sp	ecific Extravasation	Management
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# Antidote Mechanisms Explained

Understanding how each antidote works is crucial for selecting the appropriate intervention during an extravasation event. Antidotes are not interchangeable; their mechanisms of action are specific to the chemical properties of the drugs they counteract. Selecting the correct antidote enhances the chance of preserving tissue integrity and preventing long-term injury.

- **Dexrazoxane** is the only FDA-approved antidote specifically indicated for the treatment of anthracycline extravasation, such as with doxorubicin. It functions as an intracellular iron chelator. By binding to free iron, dexrazoxane prevents the formation of iron-mediated free radicals, which are responsible for the oxidative damage that contributes to ongoing tissue injury. Dexrazoxane must be administered intravenously at a new, distant site and should ideally be given within three hours of the extravasation event to be effective. Its early administration can significantly reduce the risk of necrosis and may prevent the need for surgical intervention.
- **Hyaluronidase** is an enzyme that breaks down hyaluronic acid, a major component of the extracellular matrix. By degrading this matrix, hyaluronidase increases tissue

permeability, allowing extravasated drugs to disperse more widely and be absorbed into systemic circulation. This dilution effect lowers the local concentration of cytotoxic agents, decreasing the severity of tissue damage. Hyaluronidase is most effective when used promptly after extravasation of non-DNA-binding vesicants like vincristine or vinblastine.

- **Sodium thiosulfate** acts by chemically neutralizing alkylating agents, such as mechlorethamine, through direct reaction. This neutralization forms less toxic and more easily excretable compounds, significantly limiting the extent of tissue injury. Sodium thiosulfate is administered subcutaneously in small volumes around the extravasation site to ensure widespread neutralization in the affected tissue bed.
- Dimethyl sulfoxide (DMSO) serves a dual role as a solvent and a free radical scavenger. It penetrates tissue rapidly and neutralizes reactive oxygen species generated during chemotherapy-induced tissue injury. Additionally, DMSO has antiinflammatory and analgesic properties, making it a supportive option in managing certain types of extravasation injuries. Although evidence for DMSO's use is largely based on anecdotal experience and human oncology practices, it remains a valuable adjunct for certain vesicant injuries.

Selecting and administering the correct antidote as early as possible after an extravasation event significantly improves patient outcomes. Each antidote must be matched precisely to the extravasated agent and administered using recommended routes and dosages.

## **Prevention Strategies**

Preventing extravasation events requires careful catheter placement, vein selection, slow infusion rates, constant monitoring during administration, and regular blood return verification. Staff education, simulation drills, and maintaining up-to-date extravasation kits with antidotes are also critical for prevention.

#### Conclusion

Extravasation is a preventable but serious complication in veterinary oncology. Knowledge of drug classifications, prompt recognition of symptoms, correct intervention selection, and prevention strategies together ensure the best possible outcomes for patients. Proper preparation and education are key to mastering extravasation survival skills.

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# NEW GREEN INITATIVE: Reducing the environmental impact in veterinary oncology

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## **Learning Objectives**

- Understand the concept of environmental sustainability
- Recognise the environmental impact of veterinary oncology
- Implement measures to reduce the practice carbon's footprint
- Recognise the environmental impact of volatile anaesthetic agents
- Understand the concept of low-flow anaesthesia, necessary equipment, and safe use for the patient

# Introduction

As environmental sustainability becomes an increasing priority in healthcare, it is essential for veterinary nurses to consider the ecological impact of their practices. This session will explore how various aspects of veterinary oncology, including waste disposal, chemotherapy drug management, pharmaceutical waste, radiotherapy, and anaesthesia, can contribute to environmental degradation. Through understanding the environmental impact, we can introduce strategies to reduce the practice's carbon footprint and make veterinary oncology more sustainable.

## What is Environmental Sustainability?

Environmental sustainability refers to practices that meet the needs of the present without compromising future generations. In veterinary oncology, this concept involves reducing carbon emissions, minimizing resource usage, and managing waste in a responsible and sustainable way. According to Agbafe et al. (2022), addressing climate change-related externalities in healthcare is crucial, as healthcare systems are significant contributors to global CO2 emissions. As veterinary professionals, we can apply similar principles to reduce our environmental impact.

## The NHS Sources of CO2 Emissions

The UK National Health Service (NHS) has recognized energy consumption, transportation, and waste as major contributors to its carbon emissions (NHS, 2020). While veterinary hospitals are separate from the NHS, veterinary practices similarly face challenges due to energy-intensive equipment, medical supplies, and transport. Ryan et al. (2024) demonstrate that veterinary procedures like tibial plateau levelling osteotomies, while crucial for patient care, come with substantial associated carbon emissions. Similar considerations apply to oncology care, where energy use and drug production contribute significantly to the practice's carbon footprint.

## Veterinary Hospital Waste Disposal

Waste management in veterinary hospitals is another area where sustainability must be prioritized. A study by Atiwesh et al. (2021) highlighted the environmental impact of plastic waste, which is particularly relevant to veterinary oncology, where single-use items such as syringes, gloves, and gowns are common. Proper disposal of pharmaceutical waste, including leftover chemotherapy drugs and contaminated PPE, is vital in preventing environmental contamination (Biller et al., 2016). Veterinary hospitals should implement waste segregation, recycling initiatives, and reduce reliance on single-use plastics whenever possible.

## **Chemotherapy Drugs and Pharmaceutical Waste**

Chemotherapy drugs are essential in treating cancer but are also a significant source of pharmaceutical waste. Agbafe et al. (2022) discuss the carbon footprint of pharmaceutical manufacturing, noting that drug production is a key source of CO2 emissions. Chemotherapy drugs often come in single-use plastic packaging, which adds to the growing environmental burden in healthcare settings. Furthermore, excretion of anticancer drugs and their metabolites by treated animals can contaminate the environment (Dickman et al., 2022). The long-term ecological effects of these pharmaceuticals are still being studied, but their potential harm to ecosystems must be acknowledged.

## **Radiotherapy and Environmental Effects**

Radiotherapy is an indispensable part of cancer treatment in veterinary oncology. However, it is also a significant energy consumer, and its operation contributes to the carbon footprint of veterinary practices. Baniel et al. (2024) emphasize the importance of improving the environmental sustainability of radiation therapy facilities, including optimizing energy usage and reducing the waste associated with radiotherapy equipment and radioactive waste. These changes are not only essential for improving sustainability but also for ensuring that veterinary practices remain resilient in the face of climate challenges.

#### Anaesthetic Agents and Environmental Impact

Anaesthesia, particularly the use of volatile agents like isoflurane and sevoflurane, is another major contributor to the carbon footprint in veterinary practice. These agents have a high global warming potential (GWP) and remain in the atmosphere for extended periods (Jones & West, 2019). A significant step in reducing the environmental impact of anaesthesia is adopting low-flow anaesthesia techniques. A clinical audit on low-flow anaesthesia conducted by the speaker demonstrated that reducing fresh gas flows during anaesthesia significantly lowers the environmental impact by decreasing the amount of volatile anaesthetic gases released into the atmosphere. The findings align with those of McMillan (2021), who observed that low-flow anaesthesia can be a highly effective strategy in reducing the environmental footprint of volatile anaesthetics. Additionally, a practice guide by Feldman (2012) shows how managing fresh gas flow efficiently can mitigate environmental contamination.

### Other Strategies to Reduce the Carbon Footprint

Aside from directly reducing anaesthetic emissions, there are other strategies veterinary practices can implement to reduce their carbon footprint. Promoting teleconsultations, as noted by Dickman et al. (2022), can reduce travel-related emissions, while optimizing resource use within the hospital reduces overall environmental impact. Furthermore, investing in green energy solutions, reducing waste, and creating awareness among staff are crucial to fostering a culture of sustainability. As Baniel et al. (2024) suggest, a systemic approach to sustainability in healthcare facilities—including veterinary practices—is necessary to build a more resilient and environmentally responsible future for oncology care.

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# **Genetic Signatures of Therapeutic Response in Canine Cancers**

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# Introduction

Cancer cell lines provide an important resource for exploring cancer cell biology and the preclinical assessment of therapies. Cell line drug sensitivity assays coupled with next generation sequencing modalities have helped to identify putative drivers of cancer and to link identified somatic mutations with gene expression signatures and therapeutic responses.

# Materials and methods

RNA sequencing of polyA purified mRNA from 57 cell lines of various tumor types (40 million 150 bp paired-end reads) was mapped against CanFam3.1 via STAR and normalized gene count data was generated using RUVseq. Whole exome sequencing at a depth of 200X was generated using the Agilent V2 Canine capture and short variants were called using Mutect2. Gene set variation analysis (GSVA) of transcripts was used to identify pathways enriched in each cell line. Gene expression, GSVA scores, and gene set enrichment analysis were used to identify genes and pathways associated with drug sensitivity assays for targeted agents and cytotoxic chemotherapeutics conducted using clinically relevant doses.

# Results

Putative driver mutations in known cancer genes were identified in 48 cell lines. MAP kinase activation score (MPAS) correlated with trametinib sensitivity across 33 cell lines. Using GSVA Hallmark enrichment score correlations with drug sensitivity among 13 osteosarcoma lines, Interferon Alpha Response was elevated with PARP inhibitor sensitivity, Apical junction scores were elevated in carboplatin resistant cells, and sensitivity to an Aurora A Kinase inhibitor was correlated with reduced Bile Acid Metabolism (p<0.05).

# Conclusions

Genetic analysis of canine cancer cells has identified driving mutations and gene expression signatures that may guide therapeutic treatment options.

# Using evolutionary constraint to identify functional mutations in the non-coding space of canine osteosarcoma and diffuse large b-cell lymphoma.

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#### Introduction

The non-coding part of the canine genome accounts for around 98% of the genetic sequence. Despite this, no studies have investigated the impact of somatic cancer mutations in the non-coding part of the genome in canine tumors. This is in part due to difficulties in assigning a functional role to mutations in this space. Evolutionary constraint scores (PhyloP) generated by the alignment of 241 mammals can be used to identify non-coding constraint mutations (NCCMs) which are mutations in a conserved base-pair with a putative functional role.

## Materials and methods

We analyzed paired tumor and normal whole genome sequencing data from 116 dogs with osteosarcoma (OSA) and 72 dogs with diffuse large b-cell lymphoma (DLBCL). Data was analyzed using a canine adapted Sarek pipeline to call mutations. Tumor mutations in the non-coding space were annotated using PhyloP scores and their enrichment around coding genes was calculated using a custom formula.

#### Results

Looking at the 99th percentile of genes enriched for NCCMs we identify 224 NCCM enriched genes in OSA and 85 in DLBCL. Our data show that genes enriched for NCCMs are distinct from genes affected by coding mutations, in alignment with a theory that these mutations change gene regulation without disrupting the coding gene sequence.

#### Conclusions

Our analysis identified a large set of genes enriched for NCCMs and identifies genes not previously shown to be implicated in canine OSA and DLBCL.

# A novel screening platform for personalized molecular targeted therapy in veterinary oncology

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## Introduction

Molecular targeted drugs inhibit specific molecules that are responsible for tumor growth and have demonstrated significant efficacy and tolerable side effects in human oncology. Therefore, it is necessary to identify appropriate molecular targeted drugs for each patient, even for the same tumor type but there is no established drug screening platform in veterinary oncology. Organoid cultures can develop organoids from patient-derived tumor tissues, which mimic the in vivo tumor characteristics compared to general 2D cultures. In this study, we generated patient-derived tumor organoids and evaluated the anti-tumor effects of molecularly targeted drugs.

## Materials and methods

Fresh tumor tissue samples of various tumor types were surgically removed from 116 tumorbearing dogs and cats at the Veterinary Medical Center of The University of Tokyo. Organoids were developed in original culture media and growth inhibition assays were performed using selected orally available 10 molecular targeted drugs approved for human or veterinary medicine including Abemaciclib, Alectinib, Dabrafenib/Encorafenib, Everolimus, Gefitinib, Lapatinib, Olaparib, Pazopanib, Toceranib and Trametinib.

# Results

The organoids were successfully developed in 98 % of the cases. In 112 and 94 of the 114 cases, at least one drug suppressed cell growth by at least 25% and over 50%, respectively. While organoids derived from the same tumor type tended to show similar growth inhibition patterns, each organoid displayed a distinct drug sensitivity profile.

## Conclusions

This screening platform offers a valuable test for identifying effective molecularly targeted therapies for individual canine and feline patients. Further evaluation of clinical efficacy using this screening platform would establish precision medicine in veterinary oncology.

# Evaluation of whole-body diffusion-weighted imaging for the staging of canine multicentric lymphoma

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## Introduction

Whole-body diffusion-weighted magnetic resonance imaging (WB-DWI) is a promising alternative for lymphoma staging in human medicine, providing whole-body imaging without the radiation exposure of positron emission tomography-computed tomography. WB-DWI has not yet been evaluated for lymphoma staging in dogs, where comprehensive staging currently relies on multiple imaging modalities and organ cytology. This pilot study evaluated the performance of WB-DWI for staging canine multicentric lymphoma by comparing its findings to conventional staging methods at diagnosis and following induction chemotherapy.

## Materials and methods

Five dogs with multicentric high-grade lymphoma underwent conventional staging (physical examination, complete blood count, blood smear, biochemistry panel, thoracic radiographs, abdominal ultrasound, and cytology of the liver, spleen, and bone marrow) alongside WB-DWI. Staging was performed at diagnosis and after one month of induction chemotherapy (L-COP or L-CHOP). WB-DWI findings were compared to conventional methods to evaluate its accuracy in determining disease extent and monitoring treatment response.

# Results

Conventional staging methods classified four dogs as stage IV and one as stage V (bone marrow infiltration). WB-DWI correctly identified lymph node and bone marrow involvement, but inconsistently detected liver and spleen infiltration. Following induction chemotherapy, all dogs achieved complete remission based on conventional staging. WB-DWI confirmed the resolution of lymph node and bone marrow disease in all dogs.

## Conclusions

WB-DWI demonstrates potential as a non-invasive, single examination for staging and monitoring canine multicentric lymphoma. However, additional work is necessary to improve its sensitivity for detecting liver and spleen infiltration and larger studies are warranted to validate these findings.

# A Novel Anti-CD20 mAb for Treatment of Canine B-cell Lymphoma: Pharmacokinetic and Safety Assessment

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Zoetis

# Introduction

Lymphoma is one of the most common cancers in dogs, with the B-cell immunophenotype being most common. Human Diffuse Large B-cell Lymphoma treatment outcomes have improved with the addition of a monoclonal antibody (mAb) that selectively depletes B-cells. A novel anti-CD20 mAb has been developed with specific binding to canine CD20 and potent killing of target cells in in vitro assays. The purpose of this study was to evaluate the safety and PK/PD of a novel anti-CD20 mAb in dogs.

# Materials and methods

Healthy laboratory beagle dogs (n=23), at least 4 years of age, were randomly selected to receive single or multiple doses of the anti-CD20 mAb. In vivo exposure and peripheral B-cell depletion were assessed post single- (0.2 - 10 mg/kg SC) and multiple-dose (0.05 - 0.2 mg/kg SC or IV) administration. Mechanistic modeling using serum concentrations coupled with B-cell kinetics was conducted to simulate drug effect in diseased animals.

# Results

Post SC administration, mAb showed a mean half-life of ~9.9 days and mean bioavailability of 79%. Drug was well-tolerated at the dose levels tested and no immunogenicity was observed. CD21+ B-cells in the blood started to decline an hour post-dose following single-dose administration and were completely depleted by 24 hours in all dose groups (much sooner than the tmax of 2-7 days) and this was sustained. Onset of recovery was ~50 days.

## Conclusions

Canine anti-CD20 mAb is well-tolerated in vivo at the doses tested and has good subcutaneous bioavailability. This novel mAb could significantly improve treatment options for dogs with B-cell lymphoma.

## MEDIASTINAL LYMPHOMA IN 70 DOGS TREATED WITH LOMUSTINE OR ANTHRACYCLINE-BASED MULTI-AGENT CHEMOTHERAPY: A MULTICENTER RETROSPECTIVE STUDY

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# Introduction

Primary mediastinal lymphoma is rare in dogs and associated with a poor prognosis despite treatment, most commonly with a CHOP protocol. The aims of this study were to describe the largest cohort of dogs with mediastinal lymphoma to date and assess potential prognostic factors, including the impact of anthracycline versus lomustine-based protocols on outcomes.

# Materials and methods

Data was retrospectively collected from 10 institutions. Inclusion criteria were: mediastinal mass as primary disease burden at diagnosis; cytological/histological diagnosis of intermediate-large cell lymphoma; no generalized lymphadenopathy or extra-nodal involvement (with the exception of liver and spleen); first chemotherapy treatment with CHOP/CEOP, LOP or LOPP. Median overall survival time (OST) and progression-free survival (PFS) were calculated using Kaplan–Meier. Prognostic factors were analysed via univariate and multivariable Cox or logistic regression.

# Results

Seventy dogs were included. Of cases with known outcome, 92% showed clinical response and 78% achieved complete remission. Median PFS was 113 days and median OST was 223 days, with 20% surviving longer than 450 days. CD4+/CD8- immunophenotype (p=.010), hypercalcaemia (p=.037) and chemotherapy-induced neutropenia (p=.015) were associated with longer PFS. Neutropenia at diagnosis negatively impacted PFS (p=.017) and OST (p=.004). Granular morphology (p=.023), and CD4+/CD8+ co-expression (p=.004) negatively impacted survival, whilst treatment-induced neutropenia improved survival (p=.042). Differences in PFS or OST between protocols were not significant.

# Conclusions

Neutropenia at diagnosis, granular morphology, chemotherapy-induced neutropenia and CD4/CD8 immunophenotype were associated with outcome in this cohort of dogs with mediastinal lymphoma. This is the second study associating hypercalcaemia with improved PFS in dogs with T-cell lymphoma. Overall, prognosis remains poor despite treatment; further studies are required to corroborate our findings.

# Evaluation of a multidrug chemotherapy protocol including alkylating agents for treating canine high-grade T-cell lymphoma

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### Introduction

In dogs, the treatment of T-cell lymphoma is associated with poorer outcomes compared to its B-cell counterpart. Recent studies have suggested that incorporating alkylating agents into the multidrug chemotherapy protocol may lead to improved results. This study evaluated the efficacy and potential side effects of an alkylating-rich multidrug chemotherapy protocol for the treatment of canine high-grade T-cell lymphoma, aiming to determine whether it could improve overall survival and tolerability.

#### Materials and methods

This retrospective study included chemotherapy-naïve dogs with high-grade T-cell lymphoma treated at the Utrecht University Clinic of Companion Animals with an alkylating-enriched protocol (CCNU-L(-chlorambucil)-CHOP). Response rates, disease-free period (DFD), progression-free survival (PFS), overall survival time (OST), and adverse effects of the protocol were assessed and compared to data from previously published reports. Potential prognostic factors were determined.

#### Results

Forty-three dogs with various anatomical forms of intermediate- to high-grade T-cell lymphoma were included. The overall response rate was 61.5%. Thirteen dogs (33%) achieved complete remission, resulting in a median DFP of 147 days. The median PFS and OST were 91 days and 155 days, respectively. No prognostic factors were identified. Adverse events, as indicated by abnormal laboratory or clinical pathology findings, were generally mild, with only 8.5% of the side effects classified as severe according to the VCOG-CTCAE v2 criteria.

## Conclusions

This study demonstrated that although the CCNU-L(-chlorambucil)-CHOP protocol appears to be well tolerated, the addition of alkylating agents alone failed to improve survival in our cohort. Therefore, alternative chemotherapeutic protocols should be considered.

# Computed tomography features of salivary glands neoplasia in dogs

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## Introduction

Neoplasia of the salivary glands is rare in dogs but represents a significant cause of salivary disease1. The majority of salivary gland neoplasms are malignant, with adenocarcinoma being the most commonly diagnosed histological subtype, followed by other types of carcinomas. Computed Tomography (CT) is commonly used to evaluate the head in dogs with suspected neoplasia. The objective of this study was to describe the CT features of histologically confirmed salivary gland neoplasia in dogs.

# Materials and methods

Clinical records of three UK veterinary referral centres were retrospectively searched for dogs with histologically confirmed salivary gland neoplasia that had undergone concurrent CT of the head. The CT studies were reviewed by two veterinary radiologists using a predetermined grading system.

# Results

Twenty dogs met the inclusion criteria. Carcinoma (9) was the most common histopathological diagnosis, followed by adenocarcinoma (6), acinic-cell carcinoma (2), mixed carcinoma (2) and spindle cell carcinoma (1). All the affected salivary glands were abnormal on CT with the lesions causing disruption of at least part of the gland architecture. The salivary gland lesions were typically irregular, well-defined, with cavitations and heterogenous contrast uptake. Invasion of the adjacent structures was present in 4/20 dogs. Cytology or histopathology of regional lymph nodes was performed in 14/20 cases, revealing metastasis in 2 and reactive hyperplasia in 12. All the metastatic and reactive lymph nodes were abnormal on CT. Pulmonary nodules were present in 4/20 dogs.

## Conclusions

CT is useful in the diagnosis and staging salivary gland neoplasia including the presence of invasion of the adjacent structures.

## Extracellular Vesicles from Canine Hemangiosarcoma Cell Lines as Potential Anti-Cancer Drug Delivery Systems

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#### Introduction

Canine splenic hemangiosarcoma (HSA) is an aggressive endothelial cell cancer of blood vessels, mainly affecting geriatric dogs. Splenectomy and adjuvant doxorubicin (DOX) alone or with doxorubicin-based-protocol are the most common treatment, but prognosis remains poor due to metastatic dissemination to organs (lungs, heart, liver, kidney, and brain). Extracellular vesicles (EVs), naturally secreted by almost all cells, can encapsulate different molecules, offering a promising tool for drug delivery due to their immuno-compatibility and targeting properties. This study investigates the potential of EVs derived from canine HSA patients as a DOX vehicle, to target neoplastic cells and reduce its side effects.

#### Materials and methods

Primary cell lines from spontaneous splenic HSA samples collected from owned dogs were established and phenotyped using CD31 and Factor VIII-RA antibodies. EVs were isolated from the cell medium by ultracentrifugation and size exclusion chromatography and were loaded with DOX through enhanced diffusion. The incorporation of DOX was assessed by NTA and FACS analysis. HSA primary cell lines were challenged with different concentrations of free DOX, EV-loaded DOX, and empty EVs for 4 hours, and cell viability and apoptosis were evaluated.

#### Results

Cultured spindle cells expressed Factor VIII-RA, confirming endothelial origin and demonstrating HSA culture establishment. DOX was efficiently loaded into EVs. After 4 hours of coincubation, a time-dependent increase of apoptosis and decreased viability were observed, indicating that the DOX-free or loaded-in EVs had a cytotoxic effect on the tumoral cells.

#### Conclusions

In conclusion, this pilot study highlights the potential of EVs as an innovative drug delivery system for HSA treatment.

# Preliminary Evaluation of Thalidomide as a Rescue Therapy for Canine Multiple Myeloma

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## Introduction

The first-line treatment for canine multiple myeloma (MM) relies on melphalan and prednisolone, whereas thalidomide is a first-line option in human MM. Thalidomide has been used in various canine tumours, as an antiangiogenic treatment with an excellent toxicity profile. This study aimed to evaluate thalidomide's efficacy as a rescue therapy for canine MM.

## Materials and methods

Clinical records of three veterinary referral centres were retrospectively searched for dogs with confirmed diagnosis of MM that received thalidomide as a rescue treatment. Response was assessed using Response Evaluation Criteria in Solid Tumours. Progression-free survival (PFS) and overall survival time (OST) were analysed. Toxicity was graded according to the Veterinary Cooperative Oncology Group (VCOG) Criteria for Adverse Events (AE).

### Results

Seven dogs met the inclusion criteria. Thalidomide was the first- and second-line rescue in 3/7 and 4/7 cases, respectively. Thalidomide was administered as single agent in 7/7 due to AE or MM progression. The response to thalidomide were as follows: 5/7 achieved complete response (CR), 1/7 had partial response (PR), 1/7 had progressive disease (PD). The treatment was well-tolerated with only 3/7 dogs developing VCOG grade 2 somnolence as the only AE. The median PFS was 298 days (range: 90-420 days) and median OST was 630 days (range: 450-730 days) and the.

## Conclusions

These preliminary results shows that thalidomide may represent an effective rescue therapy for canine MM. It is well tolerated, and has been shown to increase survival times, making it a potential first line strategy for the treatment of canine MM.

## Defining the mutational landscape in canine oral squamous cell carcinoma

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### Introduction

Canine oral squamous cell carcinoma (COSCC) represent the 2nd most common oral malignancy in dogs and exhibit parallels to human head and neck squamous cell carcinoma (HNSCC). However, the molecular basis of COSCC development remains poorly understood. Building on our previous results from RNA-sequencing of laser-capture microdissected regions from formalin-fixed paraffin-embedded (FFPE) tissues, we aimed to gain insight into the mutational landscape of COSCC to further elucidate the underlying molecular mechanisms.

# Materials and methods

We performed whole-genome sequencing (WGS) of tumor and matched normal tissue isolated using laser-capture microdissection from 10 COSCC archival FFPE samples. Subsequently, we catalogued the mutations identified in tumor but not matched normal tissue and compared the results to the RNA-seq data.

## Results

RNA-Seq identified 126 mutated genes in COSCC, the majority of which were validated by WGS. An additional 18'355 somatic, coding mutations with moderate to high impact (frameshifts and premature stop codons) were detected by WGS. Furthermore, the observed significant downregulation of keratins at the RNA level could be attributed to an abundance of mutations in these genes, presumably leading to loss of differentiation. 2'656 genes were recurrently mutated in at least 70% of samples, including TP63, NOTCH1, FAT1, and PIK3CA. Cross-referencing our data with the OncoKB database revealed mutations in 22 of 24 actionable oncogenes and tumor suppressor genes recurrently mutated in human HNSCC, highlighting the relevance of these alterations in oncogenic pathways across species.

## Conclusions

These data significantly extend the current understanding of COSCC and lay the basis for novel diagnostic and therapeutic approaches for affected patients.

# Factors secreted by feline oral squamous cell carcinoma cell lines enhance osteoclastogenesis and resorption, driving bone invasion

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# Introduction

Feline oral squamous cell carcinomas (FOSCC) are locally aggressive tumours that invade bone causing excessive bone resorption via osteoclasts. Identifying biomarkers for bone invasion is crucial to improve clinical outcomes. Tumour secretomes are a rich source of mediators that drive proliferation, metastasis, and invasion.

# Materials and methods

We induced osteoclast formation and bone resorption from feline bone marrow precursors with conditioned media (CM) collected from two bone-invasive and two bone non-invasive FOSCC cell lines using co-culture system and ex-vivo explant model. Proteins changes in FOSCC CM were analysed using single-shot LFQ proteomics (timsTOF-HT).

# Results

Conditioning media from bone-invasive FOSCC cell lines in the presence of CSF and RANKL significantly enhanced osteoclast differentiation from bone marrow and osteoclast resorption activity compared to CM from bone non-invasive FOSCC cell lines (p

# Conclusions

Together, our co-culture system and proteomic analysis demonstrate a robust approach for identifying the secreted factors in FOSCC cells CM potentially driving bone invasion.
# Radiotherapy as a rescue treatment for Transmissible Venereal Tumour: a retrospective study of 11 dogs.

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#### Introduction

Canine transmissible venereal tumour (TVT) is a contagious neoplasm with a favourable prognosis when treated with chemotherapy. However, in cases of chemotherapy-resistant or recurrent TVT, radiotherapy (RT) may serve as a rescue treatment. This study describes the response of TVT to RT.

#### Materials and methods

Eleven dogs with a cytological and/or histopathological diagnosis of TVT were included in this multi-institutional study. Ten out of eleven dogs received vincristine, either alone or in combination with doxorubicin. Nine dogs had tumours located on the external genitalia and two within the nasal/oral cavity. Seven dogs were treated with conformal RT (3DCRT or IMRT) and four dogs with a manual plan. A median total dose of 25.5Gy (range 12-36) was delivered in a median of 6 fractions (range 2-8).

#### Results

Complete remission was achieved in ten out of eleven dogs, while one dog experienced only partial remission. The toxicity associated with RT was minimal. Only the dog in partial remission died due to the TVT 77 days after RT. For the 10 dogs that achieved remission none developed recurrence after a mean and median follow up of 1124 and 1080 days (range 162-2216). Four dogs died for unrelated causes after 285, 730, 738, 2216 days. Four dogs were still alive and in remission at 162, 645, 1421 and 1655 days. Two dogs were lost to follow up after 1581 and 1805 days.

#### Conclusions

This study highlights that RT is an effective rescue treatment for TVT resistant to chemotherapy and can induce a complete and durable remission in most cases.

# Efficacy and tolerability of intensity-modulated radiotherapy in dogs with heart-base tumours.

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### Introduction

Only few studies describe the efficacy of radiotherapy in the management of heart-base tumours in dogs, but only with curative intent. Dogs were treated either using stereotactic body radiotherapy or highly fractionated radiotherapy. This study describes few cases treated with two alternative fractionated protocols.

#### Materials and methods

Retrospective single-institution study on dogs diagnosed with heart-base tumour treated with definitive or palliative-intent IMRT. Data collected included signalment, history, staging, diagnosis, toxicity, concurrent treatments, and outcome.

#### Results

Five dogs were included: two dogs had ectopic thyroid carcinoma, two chemodectoma, and one unspecified neuroendocrine tumour. Two dogs were treated with 12 consecutive daily fractions to a total dose of 42Gy and 45Gy. Three dogs received one or two cycles of palliative radiotherapy (14-16Gy in 4 fractions twice daily for two consecutive days). One dog was treated only with radiotherapy and four had systemic treatment, three toceranib and one metronomic chemotherapy. After radiotherapy, all dogs experienced resolution of clinical signs. At the time of maximum response, two dogs experienced partial remission, two stable disease and one progressive disease. The median follow-up time was 569 days (range 281-1647). One dog had local progression 196 days after RT, underwent a second cycle of radiotherapy and was stable 120 days later. The other four dogs were regularly monitored and progression-free after 281, 569, 1579, and 1647 days. None of the dogs developed cardiac toxicity including arrhythmias.

#### Conclusions

Fractionated IMRT protocols can be used in heart-base tumours with minimal toxicity and satisfactory efficacy. The small number of patients does not allow statistical evaluation.

# Acute Ocular Toxicity After Radiotherapy in Canine Sinonasal Tumors

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#### Introduction

Acute ocular toxicity was documented in dogs irradiated for sinonasal tumors in the past, but radiation dose constraints have not been established. We hypothesized that exceeding our recently established institutional dose constraints would be associated with a higher incidence of acute toxicity.

#### Materials and methods

Dogs with sinonasal tumors and prospective ocular examinations before and ?1x within 3 months after radiotherapy were included. Toxicity was scored with 3 systems: 1) by ophthalmologists with the McDonald-Shadduck, 2) by radiation oncologists with the VRTOG1.0 and 3) the retrospectively added VRTOG2.0 scoring system. Radiation dose was documented and adherence to our institutional ocular constraints was analyzed for each eye, retina, cornea, lacrimal and accessory lacrimal gland.

#### Results

Seventy client-owned dogs were included between 2016-2025, 241 ophthalmic examinations and radiation doses to 140 eyes and respective periocular structures were evaluated. Seventy-nine (56%), 44 (31%) and 49 (35%) eyes showed increased grade above baseline in any of the ocular structures according to the McDonald-Shadduck, VRTOG1.0 and VRTOG2.0 scoring system, respectively. Clinically relevant VRTOG1.0 grade ?2 toxicity was detected in 14 (10%) eyes and VRTOG2.0 (grade ?3) toxicity in 15 eyes (11%). No dog showed severe grade 3 VRTOG1.0 or ?4 VRTOG2.0 toxicity. In cases where our new dose constraints were adhered to (eye: D60%?15Gy, cornea: Dmax?35.4Gy, retina: Dmax?32.1Gy, lacrimal gland: Dmean?20Gy), clinically relevant VRTOG1.0 toxicity was detected in 1 (0.7 %) eye and VRTOG2.0 toxicity in 2 eyes (1.4 %).

#### Conclusions

In conclusion, the incidence of clinically relevant acute ocular toxicity was low, especially with adherence to institutional dose constraints.

# Comparative Epidemiological Study of Melanocytic Tumors in Humans, Dogs, and Cats in Portugal

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#### Introduction

Melanocytic tumors (MT) are among the most frequently diagnosed neoplasms in humans and companion animals. Despite their relevance, no previous studies have compared their epidemiology and spatial distribution across species. This study aims to bridge this gap by analyzing the incidence, risk factors, and geographical patterns of MT in humans, dogs, and cats in Portugal.

#### Materials and methods

This retrospective, cross-sectional study analyzed MT cases from the Portuguese National Cancer Registry (RON) (2011–2021) and the Portuguese Veterinary Cancer Registry (Vet-OncoNet) (2019–2023). Tumors were classified using ICD-O-3.2 for humans and Vet-ICD-O-canine-1 for animals. Descriptive statistics, incidence rate (IR) calculations, relative risk (RR) analyses, and spatial clustering - Moran's Index (Moran's I) and Bivariate Moran Local Index (BLISA) - were conducted.

#### Results

A total of 18,324 human, 1,199 canine, and 104 feline MT cases were analyzed. Melanoma, NOS was the most frequent MT in all species, whereas melanocytomas were predominantly observed in dogs. Dogs exhibited a higher IR (16.1 per 100,000) compared to humans (8.1 per 100,000) and cats (6.3 per 100,000). Breed-specific analysis identified Rhodesian Ridgebacks (RR=12.2) and Shar-Peis (RR=9.8) as the most predisposed breeds. Spatial analyses revealed significant clustering in urban areas, with human and canine cases showing strong geographical overlap (BLISA=0.345, p<0.001).

#### Conclusions

This study demonstrates striking epidemiological and geographical similarities in MT across species, reinforcing the One Health concept. Companion animals may serve as early indicators of environmental cancer risks in humans. These findings highlight the potential of comparative oncology in advancing cancer research and improving early detection strategies.

# ADOPTIVE IMMUNOTHERAPY WITH CYTOKINE-INDUCED KILLER (CIK) CELLS IN CANINE MALIGNANT MELANOMA: AN IN VITRO STUDY

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### Introduction

Adoptive Cell Transfer therapy, also referred to as cellular immunotherapy, is a new treatment approach that utilizes immune system cells to target and eliminate cancer. In this context, Cytokine-Induced Killer (CIK) cells, which exhibit both T cell and NK phenotypes with non-MHC-restricted target recognition, show significant cytotoxicity against human tumors. The aims of this study are to generate canine CIK cells and evaluate the cytotoxic effects on canine malignant melanoma (CMM) cell lines in allogenic system.

# Materials and methods

CIK cells were generated by culturing PBMC with nano-sized magnetic beads coated with anti-canine CD3 and CD28 antibodies for 14 days in medium supplemented with IFN-? and IL-2. FACS analysis at days 0 and 14 assessed CD3, CD4, CD8, CD5, and NKp46 expression. Cytotoxicity was evaluated on 5 CMM cell lines at various effector-to-target ratios (20:1, 10:1, 5:1, 2:1, 1:1).

# Results

By day 14, CIK cells exhibited high expression of NKp46 and CD8 markers, confirming the presence of both NK and cytotoxic T-cell phenotypes. Moreover, CIK cells showed significant cytotoxicity, killing an average of  $77\% \pm 11.7$  of the analysed CMM cells at effector-to-target ratios above 10:1. The cytotoxic effect progressively declined at lower ratios, highlighting their ratio-dependent killing efficiency.

# Conclusions

These findings confirm the feasibility of CIK cell therapy by effectively killing CMM cell lines in vitro, even at relatively low E:T ratios, and lay the groundwork for developing adoptive immunotherapy approaches for canine cancer treatment.

### Anti-PD1 and Intratumoral GD2-directed IL2 Immunocytokine-Augmented Radiation-Induced In Situ Vaccination Combination Immunotherapy in Companion Dogs with Malignant Melanoma

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#### Introduction

We have shown intratumoral immunocytokine (IT-IC) combined with external beam radiation therapy (EBRT) creates an in situ vaccination effect in dogs with malignant melanoma (MM), is well tolerated, has antitumor activity and alters the tumor microenvironment (TME). This trial adds immune checkpoint inhibition (ICI) to this approach. Our hypothesis is that adding ICI will be safe and result in enhanced TME modulation and antitumor efficacy.

#### Materials and methods

Six dogs with advanced local/metastatic MM, received an 8 Gy EBRT + IT-IC in situ vaccination targeting a single tumor site and 5 cycles of ICI (Gilvetmab, an anti-PD-1 given 2 weeks prior to EBRT, concurrent with EBRT and every 3 weeks thereafter). Tumor measurements and biospecimens (serum, plasma, peripheral blood mononuclear cells, tumor biopsy) were collected pretreatment and 4 times over 8 weeks after treatment. Dogs were restaged before treatment and every 6 weeks thereafter.

#### Results

The combination protocol was well-tolerated with no dose-limiting adverse events (AEs). 3 dogs experienced stable disease (SD, > 8 weeks), 2 PD, and 1 is undergoing follow-up. Four dogs eventually progressed and were euthanized at 37, 100, 184 and 355 days.

#### Conclusions

Adding ICI to in situ vaccination/IT-IC did not increase frequency or intensity of AEs. Antitumor activity is suggested by SD in 3 of 5 evaluable dogs but was not durable. Biospecimen analysis (TIL and gene expression) of TME is planned in batch at completion of follow-up. Future directions include assessment of the combination in the surgical minimal residual disease setting and dual ICI (CTLA4 and PD-1 blockade).

# Evaluating the impact of elective nodal irradiation for dogs with oral malignant melanoma undergoing hypofractionated radiotherapy

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# Introduction

Hypofractionated radiotherapy (hRT) is often used to treat dogs with oral malignant melanoma (OMM) but there is no consensus as to whether clinically uninvolved regional lymph nodes should be prophylactically irradiated. The objective of this retrospective study is to report outcomes for OMM treated with hRT with or without elective nodal irradiation (ENI).

#### Materials and methods

OMM patients undergoing hRT +/- ENI with a prescription of ?30 Gy and no evidence of metastasis were included. Fisher's exact test was used to compare development of nodal (LN-PD) and distant progressive disease (D-PD) between groups. Time to LN-PD, D-PD, overall progression-free survival (OPFS) and overall survival time (OST) were calculated via Kaplan-Meier curves and compared via log-rank test. Univariate and multivariate Cox proportional hazard models were used to estimate the hazard ratios of variables including use of ENI, WHO T stage (tumor burden and size), mitotic count, RT technique and use of xenogeneic human tyrosinase DNA vaccine.

# Results

Data from 100 dogs and 4 institutions were included; 80% had ENI and 20% did not. ENI did not statistically significantly alter either the rate of LN-PD (p=0.10) D-PD (p=0.18), or time to LN-PD (p=0.08) or D-PD (p=0.29). ENI was associated with improved OPFS (p=0.03), but not OST (p=0.27). On multivariate analysis, the only risk factor maintaining significance for OPFS (p=0.006) and OST (p=0.005) was T stage

# Conclusions

ENI did not measurably alter the oncologic outcomes for in this study population. Future investigations are planned to further clarify the role of ENI for treatment of dogs with OMM.

# Pharmacokinetics and Safety of Lysine-Specific Histone Demethylase-1 Inhibitor SP-2577 for Feline Oral Squamous Cell Carcinoma

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### Introduction

Squamous cell carcinoma (OSCC) is the most common oral tumor in cats and the prognosis with this cancer is poor, with survival times of just a few months. Lysine-specific histone demethylase-1 (LSD1) is an epigenetic regulator that promotes growth and metastasis of human and mouse OSCC. The aim of this pilot project is to establish the dosing, safety and anti-cancer properties of an oral LSD1 inhibitor, SP-2577, when administered to client owned cats with OSCC.

# Materials and methods

Three purpose bred research cats were given a single, oral dose of SP-2577 at 1mg/kg and plasma collected over 12 hours post-dosing to determine half-life, AUC and Cmax. Following the safe dosing of the healthy cats, two cats with OSCC (n=2) were dosed at 1 mg/kg and plasma samples collected over 8 hours. Based on extrapolation of lower dose PK, dosages were increased to 10 mg/kg/day (n=3), and 15 mg/kg/day (n=3). Cats were administered SP-2577 once daily for 6 weeks and evaluated 7, 14, 28 and 42 days after starting SP-2577 for exam, blood work and tumor measurements. Tumor biopsies were collected pre-treatment and day 42 or time of tumor progression.

# Results

The half-life of SP-2577 was approximately 4 hours in healthy and OSCC cats and pharmacologically active drug levels were achieved. SP-2577 was well-tolerated by the cats, and no tumor responses were noted.

#### Conclusions

SP-2577 is well-tolerated and reaches therapeutic levels in cats. Combination with other local therapies could be considered to improve tumor control.

# Evaluation of a therapeutic vaccine against the tumor vascular marker versican in dogs with invasive urothelial cell carcinoma

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#### Introduction

Invasive urothelial carcinoma (invUC) is the most common cancer of the bladder, associated with high morbidity and mortality. Current treatments offer limited effectiveness and side effects. A recently identified Gag???-domain containing splice variant of versican has been shown as a specific marker for tumor vasculature, common to solid tumors. In preclinical models, targeting this marker with a vaccine proved safe and effective. This study evaluates the safety and efficacy of an iBoost technology-based vaccine targeting versican's splice variant in dogs with spontaneous invUC. The hypothesis is that treatment with the versican vaccine, combined with COX-2 inhibition by meloxicam, will result in anti-versican antibody titers and significantly improved survival compared to a historical control group receiving carboplatin and piroxicam.

#### Materials and methods

This ongoing phase 1/2 single-arm study has enrolled 16 dogs with a minimum of six months follow-up. The treatment regimen includes four intramuscular induction vaccinations at two-week intervals, followed by maintenance vaccinations every two months, alongside daily meloxicam. Response is assessed through antibody titers, physical condition, abdominal ultrasound, and thorax X-ray.

#### Results

All dogs developed antibodies against versican following vaccination. Maintenance shots prevented titer decline, and a prolongation of overall survival was observed in vaccinated dogs compared to the historical controls. Minimal grade 1-2 injection site toxicity was noted, with no toxicity related to the antibody response.

#### Conclusions

In conclusion, the versican vaccine plus meloxicam consistently induced strong antibody responses, was well tolerated, and showed improved survival, supporting further investigation in veterinary oncology.

# Early detection of cancer using circulating tumor DNA in liquid biopsies: a first step to improve clinical care of Histiocytic Sarcoma through the follow-up of 30 Bernese Mountain Dogs

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#### Introduction

Histiocytic sarcoma (HS) is a rare but aggressive cancer in dogs, particularly affecting Bernese Mountain Dogs (BMDs), Rottweilers, and Retrievers. Due to its non-specific symptoms, HS is often diagnosed at an advanced stage, making early detection crucial for improving treatment outcomes. We previously developed a liquid biopsy assay to detect HSassociated PTPN11 mutations and explored its potential for early diagnosis.

#### Materials and methods

To assess its efficiency, we conducted a two-year follow-up study on 30 at-risk BMDs (?5 years). Plasma samples were collected every three months, and circulating tumor DNA (ctDNA) was analyzed using droplet digital PCR when HS was diagnosed. Tumor DNA was also tested for PTPN11 mutations.

#### Results

Six dogs died from HS with PTPN11 mutations. Strikingly, we detected these mutations in ctDNA an average of 6.2 months (median 5.8) before clinical symptoms appeared, with a range of 1 to 14 months. In one case, the mutation was detected 7 months before symptoms, while a CT scan two months before symptoms failed to detect HS.

#### Conclusions

These preliminary results demonstrate that our assay enables HS detection several months before clinical onset, with better sensitivity than imaging and diagnostic techniques. This early detection is an essential step toward improving management of such cancers in veterinary and human medicine.

# Characterization of somatic mutations in lymphomas of Bernese Mountain dogs

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# Introduction

Canine lymphoma exhibits many similarities to its human counterpart, making dogs a valuable model for studying the genetic mechanisms of lymphoma development. Due to the genetic homogeneity within breeds, differences in somatic mutations in lymphoma in different breeds of dogs have been observed. Bernese mountain dogs (BMDs) have a lymphoma predisposition, but somatic mutations associated with high-grade lymphoma in BMDs have not been studied to date.

# Materials and methods

Twenty-nine lymphoma samples were obtained from the Michigan State University Bernese Mountain Dog DNA and Tumor Repository. DNA was extracted using commercially available kit and sequenced using CanCan Diagnostics' TMB/MSI panel, which enriches for 499 selected genes from integral oncogenic pathways. Bioinformatic analysis was performed using custom-built analysis pipeline.

#### Results

Somatic mutations were identified in 93% of the samples in the study cohort. Findings revealed deleterious TRAF3 mutations in 26%; TP53, EP300, and MYC mutations in 22%; and MAP3K14 in 19% of the tumors. Copy number variations analysis revealed recurrent alterations in KMT2C, PIK3R1, TP53, MTAP, PTEN, MET, NRG1, PTPN11, SCRN1, and SETD2, affecting 19 of 29 cases (65%). TRAF3 was the most frequently mutated gene in our cohort of lymphomas. TP53 mutations, previously associated with a poorer prognosis, was observed more frequently than previously described. Additionally, EP300 mutations, implicated in human lymphomas but previously not reported in dogs, were identified. KMT2C emerged as the most common copy number variation in our cohort.

# Conclusions

Our findings highlight a distinct genetic profile in BMD lymphoma, aiding future treatment approaches and novel prognostic biomarkers for the breed.

# Survival outcomes of dogs diagnosed with urethral carcinoma treated with high-doserate iridium-192 brachytherapy and NSAIDs, NSAIDs alone or no treatment

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# Introduction

Canine urethral carcinomas are associated with a poor prognosis. Treatment options are limited and include non-steroidal anti-inflammatory drugs (NSAIDs), urethral stent placement, or laser ablation. Computer-planned intraluminal iridium-192 brachytherapy allows the delivery of high-dose radiotherapy while sparing surrounding tissues. The aim of the study was to compare median survival time (MST) for dogs treated with brachytherapy, NSAIDs, or no treatment.

# Materials and methods

Medical records from two referrals centers were reviewed for dogs diagnosed with urethral carcinoma between 2000 and 2023. Dogs were classified according to their treatment: Group 1 (brachytherapy, NSAIDs +/- chemotherapy), Group 2 (NSAIDs), and Group 3 (no treatment). Statistical analysis was performed using the Log-rank test and Kaplan-Meier.

# Results

A total of 27 dogs were retrospectively included in Group 1, 11 dogs in Group 2, and 7 dogs in Group 3. Among the 27 treated dogs with follow-up available at 1 month, a complete or partial clinical response was observed in 21 and 4 dogs, respectively. The MST for Group 1, Group 2, and Group 3 was 197 days (11-1097), 128 days (10-300), and 97 days (0-111), respectively. A statistically significant difference was observed only between Group 1 and Group 3. Within Group 1, the MST for dogs receiving a total dose of over 40 Gy was not significantly different from those receiving a dose of less than 40 Gy (197 vs. 98 days).

# Conclusions

Despite the small sample size, this study suggests that brachytherapy could be a valuable treatment option in the management of urethral carcinoma.

# Staging Findings in Feline Radiotherapy Candidates: Incidence and Impact on Treatment Decisions

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# Introduction

Some clinicians question the value of costly diagnostic tests beyond local tumour staging due to their low yield. However, the presence of co-morbidities may influence RT eligibility and protocol selection. This is the first study that investigated the incidence of benign and severe comorbidities and describes their impact on RT treatment in cats.

# Materials and methods

A retrospective review was conducted on client-owned cats referred to a specialist RT center between 2010-2024. Neoplastic conditions were confirmed via histopathology, cytology and for CNS tumours via CT/MRI. Staging included thoracic imaging (CT/X-rays) and when performed, abdominal imaging (AUS/CT), all reviewed by board-certified radiologists. Data on patient demographics, RT details, laboratory results, and imaging findings were collected.

# Results

A total of 82 cats met the inclusion criteria. The predominant tumours were nasal carcinoma (n=19), nasal lymphoma (n=14), and oral squamous cell carcinoma (n=13). Staging included thoracic imaging in all cases (79CT, 3X-rays), abdominal imaging in 60 cases (56CT, 4AUS), and head CT in 69 cases. Benign comorbidities were identified in 80/82 cats. Severe comorbidities altered RT protocols in 5/6 affected cats (due to lung metastases [n=2], primary liver/lung/brain mass, or multiple organ metastases), while RT was cancelled in one cat due to progressive congestive heart failure.

#### Conclusions

Benign abnormalities were detected in nearly all cats, though most lacked definitive tissue diagnosis due to clinician discretion or owner preference. While severe comorbidities were uncommon, they influenced RT decisions. These findings emphasize the importance of thorough staging in feline RT candidates to guide treatment selection and optimize patient outcomes.

# **Reirradiation of recurrent canine intracranial tumors**

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#### Introduction

Radiation therapy (RT) is the treatment of choice for intracranial tumors in dogs. The potential benefits of a second course of RT in cases of disease recurrence have been scarcely documented. This study aimed to retrospectively evaluate the long-term outcomes following a second RT course.

#### Materials and methods

Dogs with intracranial tumors were treated with a first course of definitive-intent RT, delivering 10x4Gy to the planning target volume (PTV). The second RT involved 10x4Gy or 10x3Gy to the PTV, without a clinical target volume. The study focused on the interval between the first and second RT, time to neurological progression after reirradiation, and overall survival time.

#### Results

Eight dogs (3 meningiomas, 3 gliomas, 2 pituitary tumors based on imaging diagnosis) were included. Overall mean follow-up was 982 days (range: 341-1339). Median time to first progression was 658 days (95%CI:541;776) and the mean interval between the two RT courses was 660 days (range: 266-1055). 62.5% (5/8) showed neurological worsening (compatible with late toxicity or recurrence), tumor progression was confirmed with imaging in 1/5 and median time to progression after the second RT course of 343 days (95%CI:280;407).Overall survival was 1153 days (95%CI:965;1342), with 3/8 dogs still alive at data evaluation.

#### Conclusions

Reirradiation in dogs with intracranial tumors offers a viable re-treatment option, providing a time to second progression of almost a year after the initial RT. The cumulative dose in organs at risk must be carefully considered to ensure safety. Our outlook is to propose guidelines for future documentation of reirradiated tumors in veterinary medicine.

# IL-12/IL-23 as Serum Biomarkers to Measure Response and Prognosis in Canine Lymphoma

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# Introduction

Canine lymphoma (cL) is one of the most prevalent neoplastic diseases in dogs. There is a need for more efficient and specific biomarkers to enhance the efficacy of monitoring treatment response and predicting prognosis in affected patients. The aim of this study was to investigate whether the cytokine IL12p40 could be used to measure response and prognosis in patients with cL. We hypothesised that IL12p40 would be elevated in dogs with cL, decrease with clinical treatment response, and that said elevation at diagnosis could indicate prognosis.

# Materials and methods

Levels of IL12p40 from naive dogs and their subsequent samples were analysed by ELISA in the sera of 28 dogs with cL and 24 healthy dogs. Dogs with cL were treated with a CHOP-based protocol and IL12p40 was measured at time of diagnosis, during treatment and after treatment.

# Results

There was a significant elevation (p < 0,05) at diagnosis of IL12p40 in dogs with cL compared to healthy dogs. IL12p40 followed clinical response through decreasing with clinical treatment response and increasing with progressive disease. In two dogs with cL, it showed tendencies of increasing before clinical manifestation of relapse. Results investigating the prognostic properties of naive concentrations of IL12p40 in patients were weak to inconclusive.

#### Conclusions

The findings show a promising clinical significance in using IL12p40 as a new biomarker to measure treatment response in cL patients, as well as predicting relapse before its clinical manifestation. Further research on the biomarker's ability to interpret prognosis is warranted.

# **POSTER PRESENTATIONS**

# Awareness of biosafety measures in manipulation and administration of chemotherapeutic drugs among veterinary professionals in Portugal

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# Introduction

Chemotherapy is essential in treatment of neoplasms in animals. Due to mutagenic, teratogenic and carcinogenic risks of these agents, their handling is considered an occupational hazard.

#### Materials and methods

An anonymous questionnaire, based on gold-standard safety recommendations of the American College of Veterinary Internal Medicine consensus and the guidelines of the European College of Veterinary Internal Medicine of Companion Animals, was created to evaluate awareness of veterinary professionals in Portugal (veterinarians and veterinary nurses) regarding safety protocols for manipulation/administration of chemotherapeutic drugs in companion animals.

# Results

Two-hundred responses were obtained. Most professionals were aware of the majority of the safety recommendations, namely to provide alternative positions for pregnant, breastfeeding or trying to conceive professionals (81%), prepare chemotherapy medications in a dedicated area (88%) and biosafety cabinet (72%), store chemotherapy drugs in a dedicated area (72%), use personal protective equipment (73%), use closed-system transfer devices (52%), use alternative devices to closed-system transfer devices (58%), avoid splitting or crushing chemotherapy tablets (83%), separated labeled cages for hospitalized animals undergoing chemotherapy (50,5%), correct handling of excretions from chemotherapy patients (68%), proper disposal of contaminated materials (58%) and safety recommendations to owners of animals undergoing chemotherapy (90%). However, most did not know the recommendation of periodic educational training (74%) and the content and use of a spill kit (65%).

# Conclusions

Although most professionals mentioned good knowledge regarding safety recommendations, an important number of professionals, some of which manipulate cytostatic drugs, did not. These findings emphasize the need for improvements in professional education to enhance safety standards in veterinary practice.

# Complications and outcome in six dogs with nasal planum squamous cell carcinoma undergoing nosectomy with premaxillectomy.

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### Introduction

Nasal planum neoplasia in dogs is rare, with squamous cell carcinoma (SCC) being the most common tumor, particularly, in Golden Retrievers. Advanced imaging is recommended to assess tumor extension. Treatment typically involves surgical resection, which may include adjacent bone structures. Prognosis after resection is generally favorable though relapse can occur, especially with incomplete excision. Adjuvant radiotherapy is effective but does not eliminate recurrence risk.

# Materials and methods

This retrospective study evaluated therapeutic outcomes in six male Golden Retrievers, averaging 10 years old, diagnosed with nasal planum SCC and treated with nosectomy, premaxillectomy, and cosmetic reconstruction using bilateral labial mucocutaneous flaps.

# Results

Preoperative CT scans revealed unilateral involvement in half of the cases and bilateral in the rest, with no regional or distant metastasis. Histopathology showed soft tissue involvement at the caudal margin in three dogs. One dog, treated with intraoperative electrochemotherapy and toceranib, remained disease-free for 14 months, while another with a high mitotic count recurred after two months despite treatment. The third dog had stable disease for 24 months after recurrence with toceranib.Of the three dogs with disease-free margins, none received adjuvant toceranib, and two received intraoperative electrochemotherapy, remaining disease-free for 16, 12, and 8 months. Minor surgical complications, such as suture dehiscence, occurred in three cases. All dogs had satisfactory quality of life with minimal long-term sequelae.

#### Conclusions

This study supports predisposition in Golden Retrievers, low metastatic potential of SCC, and that combined surgical and adjuvant therapies provides long-term disease control with manageable complication rates and good quality of life.

# Compliance with protocols for safe handling of chemotherapeutic drugs by companion animal veterinary professionals in Portugal

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# Introduction

Biosafety protocols protect patients, healthcare professionals and the environment from toxicity of chemotherapy drugs.

# Materials and methods

This study aimed to assess compliance with protocols for safe handling of chemotherapeutic drugs by companion animal veterinarians and veterinary nurses in Portugal, through a questionnaire based on gold-standard safety recommendations of the ACVIM consensus and the guidelines of the ECVIM-CA.

# Results

Two-hundred responses were obtained. Results revealed that most safety recommendations were not routinely implemented in most veterinary medical care centres (VMCC). Fifty-three % of responders did not prepare chemotherapy and 63% did not store chemotherapy drugs in a dedicated area, 90% did not prepare chemotherapeutic drugs in an appropriate biosafety cabinet, 56% did not use closed-system transfer devices and 40,5% did not use alternative devices to closed-system transfer devices, 83% did not have a spill kit prepared, 76% did not identify cages of chemotherapy animals, 53% did not handle correctly excretions from chemotherapy patients, 68% did not eliminate contaminated materials in clearly labeled containers and 70% indicated lack of complete coverage of safety protocols for handling chemotherapeutic drugs during academic training. Different factors contributed significantly (p

#### Conclusions

Absence of adequate infrastructure and equipment, combined with insufficient training and governance, pose significant barriers to compliance.

# Grade expectations: evaluating feline mammary carcinoma histological grading schemes

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#### Introduction

In 2015, Mills and colleagues modified the longstanding Nottingham grading system (EE) – originally developed for histological grading of human breast carcinomas – and proposed a novel grading scheme (MGS) for feline mammary carcinomas (FMC). Dagher and colleagues (2019) sought to validate these schemes (mitotic modified EE (MMEE), revised EE (REE) and MGS), but used different mitotic count thresholds. This study aims to compare each grading system with the EE framework using the original thresholds.

#### Materials and methods

208 FMC from 146 queens were graded using the EE, MMEE, REE, and MGS systems. Cohen's kappa (k) measured agreement between variable pairs. Univariate and multivariate Cox proportional hazards regression with Wald backward stepwise method assessed the 3year prognosis in 79 queens.

#### Results

Crosstabulation showed that FMC EE grades II and III were mostly downgraded to MMEE and REE grades I and II, respectively. Agreement between these schemes was poor to slight (kEE/MEE=-0.031, kEE/REE=0.039). Regarding the MGS grades, EE grade II were largely allocated to MGS grades I and II, whereas EE grade III chiefly remained in MGS grade III. A fair agreement was observed (kEE/MGS=0.317).Univariate overall survival analysis was statistically significant (p

### Conclusions

A consensus on the optimal grading scheme and mitotic count thresholds for diagnostic use in FMC are essential, as they greatly impact the resulting grades and prognosis.

# Old roots, new branches: a comparison of feline mammary tumor classification systems

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#### Introduction

The 2019 edition of the histological classification of feline mammary tumors (FMT) (Zappulli et al.) provides new information on descriptive morphology, differential diagnosis, and prognosis. Our goal was to compare this classification to the 1999 classification (Misdorp et al.) regarding lesions' frequency and prognostic value.

#### Materials and methods

307 FMT from 185 queens were evaluated according to the 1999 and 2019 histological classifications. A three-year survival analysis was assessed in 82 queens by Kaplan-Meier curves and log-rank tests.

#### Results

Similar proportions of non-neoplastic lesions, benign and malignant tumors were obtained, irrespective of the classification system. Duct ectasia with mammary cysts was the most frequent non-neoplastic lesion. While simple adenoma was previously the most frequent benign tumor, ductal adenoma was more frequent according to the 2019 classification. Tubulopapillary carcinomas (TPC) followed by solid carcinomas (SC) were the predominant malignant neoplasms, regardless of the classification system. Crosstabulation of the most frequent lesions revealed that TPC, as defined in 1999, were mostly redistributed into TPC, intraductal papillary carcinoma and comedocarcinoma when following the 2019 classification. SC were mainly categorized as SC and comedocarcinoma, and most cribriform carcinomas were reclassified as tubular carcinomas. The 2019 classification was significantly associated with overall survival (p=0.034). Queens with ductal-associated carcinomas had significantly longer survival times than others. No significant associations with survival were found regarding the 1999 classification.

# Conclusions

The 2019 classification for FMT improved on detail of descriptions and images, enabling finer subtype stratification, and showed a significant association to overall survival, unlike the 1999 classification.

# Retrospective Analysis of Hypofractionated Volumetric Modulated Arc Therapy for Canine Primary Lung Tumors

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### Introduction

This retrospective case series evaluates conformal and homogeneous target coverage, efficacy and side effects of hypofractionated volumetric modulated arc therapy (HF-VMAT) for primary lung tumors (PLTs) in dogs, including treatment of multiple lesions.

# Materials and methods

Ten dogs that received HF-VMAT for PLTs were evaluated. Data collected included signalment, diagnosis, RT prescription, side effects (graded per VRTOG v2.0), dosimetric parameters, and progression.

# Results

The most common tumor type was carcinoma (n=8). Four dogs received once-weekly 7–8 Gy/fraction (4 total), while six received once-daily 4 Gy/fraction (total 20 Gy). One dog was treated twice, totaling 11 RT plans. Plans were calculated using Acuros XB with 6MV flattening filter-free photons. Gross tumor volume (GTV) included a single mass in four plans and multiple lesions (2–9) in seven plans. Median GTV was 95.9 cm<sup>3</sup> (range: 1.6–408 cm<sup>3</sup>). Mean Conformity Index and Homogeneity Index were 0.99±0.019 and 0.105±0.091, respectively. Clinical signs improved or resolved in four of seven dogs within a median of 15.5 days. Acute Grade 1–2 lung toxicity occurred in four of nine dogs; in three, it was incidental on radiographs, and two had multiple lesions treated. Late fibrosis, noted only on radiographs, developed in two of six dogs. GTVs were smaller at last RT (median reduction 20%, range: 1–77%). Median progression-free survival was 121 days (range: 9–235).

# Conclusions

HF-VMAT for canine PLTs was well tolerated, providing good target coverage, tumor response, and symptom relief with low toxicity, even in cases with multiple lesions. More cases are needed to validate these findings.

# Clinico-pathological and prognostic significance of COX-2, CD44, and PD-L1 expression in cats with exocrine pancreatic carcinoma

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#### Introduction

Exocrine pancreatic carcinoma (PC) is a rare cancer in cats associated with a poor prognosis. Although a minority of cats can experience long-term survival, there is a need to better understand the biology driving PC progression and identify prognostic biomarkers. The main aim of this study was to assess the expression of CD44, PD-L1, and COX-2 in cats with PC. A secondary aim was to investigate associations between overall immunohistochemical scores (OIS) and histological characteristics, metastasis and survival.

#### Materials and methods

Formalin-fixed paraffin-embedded PC sections from cats diagnosed between 2001-2021 submitted to three laboratories were reviewed and immunohistochemical labelling for CD44, PD-L1, and COX-2 was performed. The product of cell immunolabelling percentage and intensity was used to generate the OIS. Clinico-pathological, staging, treatment, and outcome data were recorded.

#### Results

Forty cats were included. CD44 was expressed in all PC samples with 27 (67%) cats showing moderate to high OIS. COX-2 and PD-L1 expression were seen in 18 (45%) and 20 (50%) cats, respectively. Clinical records from 27 cats were available for review. Metastasis was present in nine cats and median survival time was 7 days (range 1 –1094), with a 1-year survival rate of 13.8%. No statistical associations were found between CD44, PD-L1, COX-2 expression and histological subtype, necrosis, vascular invasion, mitotic count, presence of metastasis or survival.

#### Conclusions

CD44, PD-L1 and COX-2 were often expressed in cats with PC. Further investigation is needed into the prognostic and possible therapeutic role in a larger cohort of cats.

# The Molecular Landscape of Canine PWT and PNST: New Insights into Subtype Diversity and Target Discovery

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#### Introduction

Canine perivascular wall tumors (PWTs) and peripheral nerve sheath tumors (PNSTs) are prevalent soft-tissue sarcoma (STS) subtypes in dogs. Current therapies rely on surgical removal, yet recurrence and mortality rates remain high due to challenge of accurately defining tumor margins, resulting in incomplete resections. Improved diagnostic precision and novel therapeutic approaches, including targeted therapies or tumor visualization modalities, are hindered by limited molecular insights into STS subtypes.

#### Materials and methods

To address this shortcoming, we performed spatially defined proteomic and transcriptomic profiling of 19 PWTs, 26 PNSTs and matched PTT using laser-capture microdissection followed by RNAseq and LC-MS/MS.

#### Results

We identified 5,617 proteins across 108 tissue samples and 13,788 transcripts in 104 tissue samples, including tumor, skeletal muscle, connective, and adipose tissue. Principal component analysis and unsupervised hierarchical clustering effectively separated the four tissue types in both datasets, with tissue type being the primary source of variability. Combined transcriptomic analysis revealed significant molecular heterogeneity, identifying the existence of two molecular subclusters within the PNST spectrum characterized by differences in identified gene fusions and the presence of yet undefined subtypes within this cohort. Differential gene expression analyses identified tumor-specific targets across subclusters, with shared upregulated genes offering potential as diagnostic, therapeutic, and visualization markers.

#### Conclusions

This study provides a detailed molecular characterization of canine PWTs and PNSTs, identifying novel subtypes that diverge from histopathological diagnoses. Findings underscore the value of molecular profiling to refine tumor classification and guide the development of targeted therapies and visualization tools, with implications for improving clinical outcomes.

# Laparoscopic Adrenalectomy in a Cat Diagnosed with Pheochromocytoma

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#### Introduction

Pheochromocytoma is an uncommon neuroendocrine tumor of the adrenal medulla in cats, associated with excessive catecholamine secretion and nonspecific clinical signs related to hypertension. This report describes the diagnosis and successful laparoscopic adrenalectomy in a cat with pheochromocytoma.

#### Materials and methods

A 14-year-old neutered male European Shorthair cat was presented for a geriatric checkup, with hypertension as the main clinical sign. A diagnostic workup, including bloodwork, urinalysis, abdominal ultrasonography (AUS), and computed tomography, revealed a 2.22 × 1.60 × 2 cm right adrenal mass without evidence of caudal vena cava invasion or metastasis. Fine-needle aspiration puncture suggested a neuroendocrine tumor. ACTH testing, aldosterone, and plasma normetanephrine levels were evaluated, with the latter being elevated, suggesting pheochromocytoma as the most likely diagnosis.

#### Results

Preoperative management included prazosin (0.5 mg/8h) and amlodipine (0.25 mg/kg/24h). A laparoscopic right adrenalectomy was performed using a three-port technique with meticulous dissection to minimize vascular complications. Adrenal vessels were ligated with titanium clips, and the gland was retrieved using a specimen bag. Transient intraoperative complications occurred during gland manipulation, including ventricular tachycardia and hypertension. Hypertension resolved within 24h, and the cat was discharged 48h postoperatively. Histopathological analysis confirmed pheochromocytoma. Follow-up, including thoracic radiographs and AUS every 3 months, showed no recurrence at 543 days post-surgery.

#### Conclusions

Laparoscopic adrenalectomy has proven to be a minimally invasive, precise, and safe procedure. To the best of the authors' knowledge, this is the first reported case of feline pheochromocytoma successfully treated with this technique. Further studies are needed to evaluate long-term outcomes and refine surgical protocols.

# Single-cell RNAsequencing illuminates cellular and molecular heterogeneity of canine soft-tissue sarcomas

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#### Introduction

Soft-tissue sarcomas (STS) are a heterogeneous group of frequent mesenchymal tumours in dogs. Despite aggressive surgery, chemo- and radiotherapy, 20–30% of affected dogs succumb due to local recurrence or metastasis. The development of adjuvant targeted therapies and immune checkpoint inhibitors (ICI) could improve outcomes, but progress is hindered by a lack of detailed understanding of canine STS and its tumour microenvironment at the single-cell level.

#### Materials and methods

To assess intratumoral heterogeneity and the interplay between different cell types, we characterize 11 freshly excised canine STS (1 fibroma, 2 myxosarcoma, 2 STS NOS, 1 spindle cell sarcoma, 3 PWT and 2 PNST) and 7 matched normal tissue using single-cell RNA sequencing (scRNAseq).

#### Results

The analysis yielded data of 93'377 cells from tumour tissue and 53'210 cells from normal tissue, which could be differentiated into 10 different cell clusters including tumour cells, fibroblasts, various immune cell subtypes, such as macrophages, T and B cells, endothelial and smooth muscle cells. Cell-cell interaction analysis predicted a strong interaction between macrophages and dendritic cells. In contrast, T cells showed no evidence of interaction with tumour cells, highlighting a crucial role for immune evasion in STS development, a notion that was supported by tumour-specific downregulation of genes involved in adaptive immune response, cytokine response and leukocyte migration.

#### Conclusions

By delivering a detailed overview of cellular heterogeneity and transcriptomic changes in tumour compared to normal tissue, this study provides the first scRNAseq data on canine STS and highlights a crucial role for macrophages in immune evasion of these tumours.

# Class II MHC as a predictor of outcome in canine B-cell lymphoma

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#### Introduction

Flow cytometry (FC) is commonly used to immunophenotype canine lymphoma. In human Bcell lymphoma, low class II major histocompatibility complex (MHCII) expression is reliably associated with poorer outcome, thought to be caused by reduced immunosurveillance. MHCII is normally highly expressed in canine B-cell lymphoma. Several studies have investigated the prognostic significance of MHCII expression in canine B-cell lymphoma comparing median fluorescence intensity, but no consensus exists. We hypothesised that percentage of cells expressing MHCII on FC would be prognostic in canine B-cell lymphoma. A secondary aim was to investigate associations between outcome and other aberrantly expressed FC antigens.

#### Materials and methods

A single-centre retrospective review of hospital records (2016-2023) for cases of canine multicentric B-cell lymphoma treated with a 19-week CHOP protocol. Expression of FC antigens CD3, CD3-12, CD4, CD5, CD11d, CD21, CD34, CD45, CD79a and MHCII was recorded. Median overall survival time (OST) was calculated using Kaplan-Meier and associations between FC antigen expression and survival were assessed using the log-rank test.

#### Results

Fifty-two patients included. Median OST was 265 days. There was no statistically significant difference (P

#### Conclusions

Percentage of cells expressing MHCII using logical cut-off values was not significantly associated with overall survival. Further multicentre studies are required to investigate prognostic significance of MHCII- expression and other aberrantly expressed FC antigens.

# Liquid Biopsy, Lipidomics, and Artificial Intelligence for the Diagnosis and Phenotyping of Canine Lymphoma

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#### Introduction

Canine lymphomas pose a significant clinical challenge due to their aggressive behavior and high relapse rates, particularly in T-cell lymphomas. Relapse is associated with a poor prognosis. Accurate and timely diagnostic tools, alongside effective strategies for monitoring relapse, are urgently needed. Liquid biopsy-derived lipidomics, coupled with artificial intelligence (AI), offers a promising avenue for developing robust, non-invasive diagnostic methods.

#### Materials and methods

Plasma samples from 52 dogs (32 with lymphoma, 20 healthy controls) were analyzed using MALDI mass spectrometry, a technique characterized by its straightforward sample preparation, making it suitable for clinical applications. Lipid and metabolite profiling yielded approximately 350-600 lipids per spectrum. Data preprocessing involved variable selection through ANOVA, reducing the dataset to ~10% of lipid species for further analysis. Diagnostic patterns were then identified using principal component analysis (PCA) and machine learning algorithms.

#### Results

Multivariate PCA analysis revealed three distinct clusters: Cluster A (T-cell lymphomas), Cluster B (B-cell lymphomas), and Cluster C (healthy controls), with no overlap between clusters. Machine learning models trained on selected lipidomic variables demonstrated high diagnostic performance, achieving sensitivities and specificities above 90%. These findings highlight the potential of integrating lipidomics and AI to accurately diagnose and phenotype lymphoma cases.

#### Conclusions

This study demonstrates the potential of combining liquid biopsy, lipidomics, and AI to develop a novel diagnostic test for lymphomas. This approach enables simultaneous diagnosis and phenotyping, providing a non-invasive alternative suitable for early detection. Future research will focus on enhancing minimal residual disease detection.

# Long-term response of electrochemotherapy as sole treatment in a cat with metastatic lower lid mast cell tumor

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#### Introduction

In cats, mast cell tumors arising in anatomically intricate regions of the head pose considerable challenges to achieving therapeutic outcomes that are both effective and safe. Surgical intervention is often not feasible, as it may disrupt critical structures or cause functional impairment. Electrochemotherapy has been identified as a minimally invasive alternative, providing effective local tumor control while preserving adjacent tissues.

#### Materials and methods

A seventeen-year-old spayed female domestic shorthair cat was presented for a progressive mass of approximately 2.5 cm growing on the lower eyelid. A cytopathological exam yielded a diagnosis of a well-differentiated mast cell tumor. Surgical removal of the ipsilateral submandibular lymph node was decided after complete staging procedures and confirmed metastatic following histopathological examination.

#### Results

Two sessions of electrochemotherapy were performed at three-week intervals using intratumoral and systemic bleomycin. The treatment was well tolerated and the cat achieved complete remission. Electrochemotherapy provides effective local control and should be considered as an alternative to extensive surgery with local sensory and functional complications.

#### Conclusions

This procedure is a safe and effective option for mast cell tumors, and further investigation is warranted to standardize its use. Systemic or local toxicities were not detected during the entire course of therapy. Three years post-treatment, the cat remains in complete remission, without any impact on its sight.

# Faecal microbiota correlates with prognostic and clinicopathological features in dogs with mast cell tumours

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#### Introduction

Mast cell tumours (MCT) are the most common cutaneous cancer in dogs. Like in humans, indolent and aggressive forms have been described and the therapeutic options are limited, highlighting the importance of discovering other cancer-promoting factors. Evidence has emphasized the impact of the microbiota in oncological diseases; therefore, the aim of this study was to assess if the faecal microbiota in canine MCT could influence the disease pathogenesis and patient's outcome.

#### Materials and methods

Using 16S rRNA gene sequencing, the faecal microbiota was characterized in 56 dogs, 28 healthy and 28 with MCT. Bioinformatic analyses with Python were performed using a DADA2-based pipeline and models with T-test, ANOVA or chi-squared test that were applied to identify taxonomic groups associated with prognostic and clinicopathological features.

#### Results

Multiple bacterial genera revealed significant differences when stratifying by diseased versus healthy dogs, histologic subtype and grade, tumour size, metastasis, overall survival (OS) and disease-free survival (DFS). An increased abundance of Proteobacteria was found in patients with higher tumour size (p=0.03), lower DFS (p

#### Conclusions

This study was the first to provide insight into faecal microbial profiles associated with MCT clinicopathological features and patient's prognosis, highlighting the prognostic and potential therapeutic value of microbiome in oncological diseases.

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# Treatment of feline nasal carcinomas with chemotherapy: a multi- institutional retrospective study

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#### Introduction

Carcinomas are the second most common feline intranasal neoplasm. Various treatment options, including RT, surgery or a combination of both have described for nasal carcinoma (NC) but data regarding outcome with medical therapy are lacking. The aim of this retrospective study was to evaluate the outcome of cats with NC treated with medical therapy.

#### Materials and methods

Cats with histological or cytological diagnosis of NC treated with chemotherapy and/ or tyrosine kinase inhibitors were enrolled. Response to therapy, median time to progression (MTTP) and median survival time (MST) were described. MST of treated cats was compared with MST of a control group receiving palliative therapy alone. Survival outcomes was estimated with Kaplar-Meier method and differences between groups was assessed with Log-rank test. Analyzed clinical variables possibly associated with outcome included type of clinical signs at diagnosis, presence of epistaxis, facial deformation, stage, type of treatment, use of NSAIDS and previous surgical debulking. Significant p value was set at 0.05.

#### Results

Eighteen treated cats were enrolled in the study. Fifty percent had stable disease, 30 % progressive disease and 20 % partial remission. MTTP was 160 days and MST was 185 days. MTTP and MST of treated patients were not statistically different from 15 untreated patients (p 0.47). The only clinical variable associated with survival was the type of clinical signs at diagnosis (p < 0.0088).

#### Conclusions

Medical treatment did not improve the outcome of cats with NC. Further studies with a larger number of subjects homogeneously treated are needed.

# Atypical Metastasis of Feline Mammary Carcinoma to the Sciatic Nerve: A Case Report

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#### Introduction

Feline mammary carcinoma (FMC) metastases (clinical stage IV) occur predominantly in lungs, pleura and regional lymph nodes, yet their clinical management is poorly documented. Additionally, reports addressing atypical metastatic locations and their clinical implications remain scarce

#### Materials and methods

A 10-year-old domestic shorthair cat presented with three nodules in the right mammary gland (second thoracic and both abdominal mammary glands). Clinical staging revealed no evidence of distant metastases, and the cat underwent a right radical mastectomy with inguinal lymphadenectomy. Histopathological analysis identified a micropapillary grade II carcinoma with vascular invasion in all mammary nodules and inguinal lymph node metastases

#### Results

Six-months post-surgery, the cat exhibited lameness and severe muscle atrophy in the right pelvic limb. Computed tomography identified a mass involving the right iliac body, extending to the right iliac artery and potentially affecting the sciatic nerve. No additional distant lesions were detected. Fine-needle aspiration cytology of the iliac mass suggested a carcinoma lesion. Medical management was focused on pain control, with disease progression monitored through serial imaging. The cat's condition deteriorated with multiple other metastatic lesions, leading to euthanasia five months later. The necropsy findings confirmed the presence of metastatic lesions in the sciatic nerve, gluteal muscles, pubic bone, lungs, urethra, and bladder

#### Conclusions

This case highlights the aggressive nature of FMC with an unusual metastatic pattern, underscoring the importance of considering atypical metastatic sites during clinical evaluation. These findings aim to raise awareness among veterinary oncologists about the need for comprehensive diagnostic approaches and individualized management strategies for advanced FMC cases

# Unique Presentation of Canine T-zone Lymphoma with Nervous System Involvement

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#### Introduction

T-zone lymphoma (TZL) is the most common subtype of canine indolent lymphoma. TZL is characterized by the loss of CD45 expression and a unique histologic and cytomorphologic pattern. The most common clinical abnormalities are ?1 enlarged lymph node and/or lymphocytosis Our patient had enlarged cervical lymph nodes associated with involvement of the nervous system, which is a unique presentation.

# Materials and methods

A neutered female Havanese was referred to our clinic to explore cervicalgia. MRI revealed multifocal lesions near the C4-C5 vertebrae: intramedullary and paraspinal muscle lesions, and a mass effect near the oesophagus. Fine needle aspiration and immunophenotyping of the lesions were performed.

# Results

Morphological criteria supported a diagnosis of T-zone lymphoma, confirmed by the loss of CD45 expression. Blood work highlighted lymphocytosis and moderate elevation of hepatic enzyme activity. Due to the involvement of the nervous system, a chemotherapy protocol with Lomustine and prednisolone was chosen. After four cycles, follow up showed a complete regression of adenopathy, a very significant regression of nervous lesions and a normal lymphocyte count. The treatment was adjusted by switching from Lomustine to Chlorambucil. A follow-up MRI performed three months later showed stable disease.

#### Conclusions

This case of neurological involvement TZL provides insight into this unique location. Immunophenotyping through flow cytometry is an easy technique to differentiate indolent TZL from more aggressive T-cell neoplasms. Alkylating agent with the better central nervous system penetration was chosen, but description of additional cases will help to improve a better therapeutic strategy for these patients.

# Cannabinoid Receptors Expression (CB1R, CB2R) in Canine Amelanotic Oral Melanoma: preliminary results

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### Introduction

Cannabinoid receptors (CB1R and CB2R) are integral components of the endocannabinoid system, known to influence various cancer mechanisms such as angiogenesis, apoptosis and also reducing nociception. Canine oral melanoma, particularly the amelanotic subtype, are highly aggressive with limited prognostic. Given the urgent need for novel therapeutic targets, this study aims to evaluate the expression of CB1R and CB2R receptors in canine amelanotic oral melanoma in order to explore potential immune-check points, that could help limit the tumor dissemination and improve patient welfare.

# Materials and methods

Indirect immunohistochemistry was performed on 20 amelanotic oral melanoma samples previously identified using melanocytic markers, including Melan-A. CBR1 (Origen® 1:100) and CBR2 (Abcam® 1:200) antibodies were incubated overnight. A positive neoplastic tissue was scored for intensity using a semi-quantitative system ranging from zero (negative) to three (very intense). Inflammatory cells and epidermis were used as a positive internal control.

# Results

CB1R expression was minimal (

# Conclusions

The absence of CB1R and the strong expression of CB2R in canine amelanotic oral melanomas suggest a potential role for CB2 as an immune-check point for tumor treatment. These findings contribute to understanding the prognostic significance of CB2 in canine oncology and support the use of dogs as translational models for studying cannabinoid receptor pathways in human cancers. Continued research in this area could uncover new insights into the role of cannabinoid receptors in cancer biology and therapy.

# **COX-2 Expression in Canine and Feline Bile Duct Neoplasms**

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#### Introduction

Cholangiocarcinomas (CCA) are malignant neoplasms arising from the biliary epithelium and are relatively common in humans, cats and dogs. Surgical resection if clinically feasible is the treatment option with a very low success rate. COX-2 is an enzyme that is neoexpressed in different tumours and those neoexpressing this enzyme are candidates for COX-2 selective-inhibitor treatments. To the author's knowledge this is the first study addressing the expression of COX-2 in canine and feline bile duct neoplasms (BDN).

#### Materials and methods

Twenty canine (19 CCA, 1 cholangioma (CL)) and seventeen feline (14 CCA, 3 CL) BDN were immunohistochemically stained with a monoclonal anti-COX2 antibody. A semiquantitative scoring system (percentage of positive cells and immunolabeling intensity) was used. COX-2 was compared with histological subtype, mitotic count (MC), necrosis, inflammation, desmoplasia, and lipidic change. Statistical analysis (correlation matrix and unpaired student t-test) was performed with statistical significance set at P<0.05.

#### Results

COX-2 is not expressed in normal liver parenchyma. A range of both benign and malignant biliary neoplastic lesions neoexpressed COX-2. COX-2 was neoexpressed in 85% of canine and in 60% of feline CCA respectively. COX-2 expression was not associated with histological subtype, mitotic count, necrosis, inflammation, desmoplasia, or lipid change (p>0.05). Intravascular neoplastic emboli and metastatic lesions also expressed COX-2 with a similar immunolabeling as the primary neoplasm.

#### Conclusions

COX-2 was neoexpressed in a significant proportion of canine and feline CCAs suggesting it is involved in bile duct tumorigenesis. We hypothesize that COX-2 could be a potential therapeutic target in canine and feline CCA.

# Palliative Radiotherapy for Canine Carotid Body Paragangliomas: Case Series

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#### Introduction

Carotid body paragangliomas (CBP) are rare neuroendocrine tumors that are characterized by extensive local invasion. Surgical excision therefore carries significant risk of perioperative morbidity. Limited evidence exists on the use of palliative-intent radiation therapy (RT) for managing CBP. This case series evaluates the clinical outcomes and adverse effects of palliative-intent RT for the treatment of CBP in dogs.

#### Materials and methods

Four dogs with CBP were treated with palliative-intent RT [4-5 fractions of 4-5Gy, 20-25Gy total dose prescribed to the planning target volume (PTV)]. One dog underwent a second course of palliative-intent (5 x 5Gy, total dose 25Gy). Three dogs were treated with volumetric-modulated arc therapy and one dog with 3D-conformal RT. Radiation adverse events (AEs) were evaluated using VRTOGv.2 criteria, and tumour response was assessed using RECIST.

#### Results

Diagnosis was based on computed tomography and cytology in all dogs. For the 2 dogs with objective response assessment, one dog had a partial response and the other had stable disease. Acute AEs were limited to grade 1 or 2 pain, tracheitis and esophagitis. No clinically relevant late AEs were observed. Two dogs were euthanized due to progressive disease 10 and 12 months following RT, and 2 dogs are still alive 10 and 26 months following RT.

#### Conclusions

Palliative-intent RT may be a viable therapeutic alternative in dogs with unresectable or invasive CBP. Additional studies to evaluate altered dose, fractionation, and AEs are warranted.
# Use of toceranib phosphate (Palladia®) as the first therapeutic option for urothelial carcinomas in dogs - a case study

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### Introduction

With the search for more targeted ways of treatment with fewer associated adverse effects, the use of tyrosine kinase inhibitors, such as toceranib phosphate, has been transposed from human to veterinary medicine. Toceranib phosphate is authorized only for the treatment of certain canine mastocytomas types but has been shown to be beneficial in other neoplasms types, such as urothelial carcinomas, a disease that accounts for around 1% of all canine neoplasms. This study evaluated the efficacy of toceranib phosphate as a first therapeutic option in urothelial carcinomas.

### Materials and methods

The study included 13 canines, predominantly females, neutered/sterilised, of the Beagle breed and with an average age of 11 years, followed by the Oncology department of the Veterinary School Hospital of the Faculty of Veterinary Medicine of the University of Lisbon, with urothelium carcinoma and treated with toceranib phosphate. The doses of toceranib phosphate used ranged from 1,9 to 2,75 mg/kg, administered every other day and associated with a non-steroidal anti-inflammatory drug.

### Results

More than half of the animals showed a positive response to the treatment, keeping the disease stable for an average of 242.4 days. The average survival time was 203,1 days, with most of the animals dying due to the progression of the disease.

### Conclusions

The results obtained suggest that toceranib phosphate might be a promising therapeutic option for urothelial carcinomas, highlighting the importance of further research. This approach could improve the quality of life of affected dogs and expand the therapeutic options available in the field of veterinary oncology.

# Management of canine ectopic sublingual thyroid carcinoma by combination of basihyoid cartilage amputation followed by IMRT-based radiotherapy : 3 cases

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### Introduction

Treatment of ectopic thyroid tumour in the dog is challenging especially due to the localization of the tissue, most commonly next to the basihyoid cartilage. Radioiodine treatment is limited by its availability, radiation exposure of medical workers and the possible persistence of respiratory and hyperthyroidism-related signs. We describe the clinical features and management of 3 dogs treated by combination of a radical cartilage excision and radiotherapy.

### Materials and methods

All 3 dogs underwent a complete staging of their disease with tomodensitometry, assessment of their thyroid function by blood testing and scintigraphy before surgery and were followed until death by reassessment of thyroid function and repeated tomodensitometry exams.

### Results

2 on 3 dogs were hyperthyroid at presentation and no dog developed metastasis throughout the study. All dogs underwent complete amputation of the basihyoid cartilage with the ectopic thyroid carcinoma without any postoperative complication. Intensity modulated radiation therapy was performed with a hyperfractionnated protocol (15 seances of 3 Gy) One dog developed a recurrence 22 months after first treatment and was re-operated with adjuvant radiotherapy. This dog died 20 months after 2nd surgery due to unrelated cause and the 2 other dogs are alive at the time of writing (respectively at 6 months and 37 months after surgery) without recurrence neither hyperthyroidism.

### Conclusions

We described the long-term follow-up of 3 dogs treated for ectopic thyroid carcinoma with cartilage amputation followed by radiotherapy with presentation of tomodensitometric or scintigraphic features before and after surgery.

# DIFFERENCES OF CD45 EXPRESSION BETTWEN TUMORAL B CELLS AND NORMAL LYMPHOCYTES IN DOGS

Víctor Domingo Roa, Ana Tejada Roa, Laura Sanjuan Nuñez

Atypia, Oncología Veterinaria y Experimental

### Introduction

CD45 is a major glycoprotein expressed on all nucleated cells of the immune system and in several types of lymphoid neoplasms. In particular, CD45 serves as an important diagnostic and prognostic marker and plays a key role in the immunophenotyping of lymphoid neoplasms. The aim of this study was to evaluate differences in CD45 expression in B-cell malignancies such as large B-cell lymphoma (LBCL), chronic B-cell lymphocytic leukaemia (B-CLL) and normal lymphocytes (B and T) present in the same samples.

### Materials and methods

Sixty-seven dogs diagnosed with LBCL or B-CLL were evaluated by flow cytometry using the following panel: CD45/CD21/CD3/CD5/CD4/CD8/MHCII/Ki67/CD34.

### Results

Fifty-seven dogs (57/67, 85%) were classified as LBCL (CD45+/CD21-/CD3-/CD5-/CD4-/CD8-) and 7 (7/67, 15%) as B-CLL. The mean CD45 expression was 30,626.96 RFUs (4,548.13-57,581.35) for LBCL and 18,319.68 RFUs (5,288.87-28,453.36) for B-CLL. Mean CD45 expression was 53,543 RFUs (156,480.15-8,673.60) for normal T lymphocytes and 19,467.32 RFUs (53,495.54-2,973.76) for normal B lymphocytes.LBCL and CLL showed significantly different levels of CD45 expression (p

### Conclusions

As the understanding of CD45 biology evolves, its role as a prognostic marker or its future as a therapeutic target could potentially improve patient outcomes.

# Minimising variability of preanalytical factors is key to successful cfDNA testing

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# Introduction

Circulating cell free DNA (cfDNA) is a promising analyte for detecting pathological processes before the clinical signs of a disease appear. However, cfDNA is a relatively unstable macromolecule and many preanalytical factors can affect its concentration. In this study, our findings outline the most important preanalytical factors and their effects on canine cfDNA testing from blood.

# Materials and methods

Over 3,000 dogs were recruited to this study with informed owner consent. Blood samples were collected from healthy dogs and dogs diagnosed with a variety of clinical diagnoses. Multiple conditions were tested for sample collection, transport, and reception steps. Different blood tube types, plasma separation protocols using centrifugation, cfDNA extraction methods, and DNA QC approaches were compared, and the best approaches were combined into a laboratory workflow.

# Results

The most critical factors affecting the plasma cfDNA quality and quantity were found to be the extent of haemolysis and WBC contamination. These were followed by storage and transport temperatures, and the tube type used in blood collection. In contrast, the presence of lipids was not found to have a significant effect. cfDNA yield was also relatively stable across different plasma separation protocols.

# Conclusions

cfDNA has the potential to revolutionise the diagnosis and monitoring of many diseases, and it is essential to standardise preanalytical factors as much as possible to ensure high-quality results.

# Primary urethral leiomyosarcoma in a cat – a case report

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### Introduction

Lower urinary tract tumours are rarely described in cats. The most frequent one is transitional cell carcinoma. Most of the tumours that affect feline urethra are primarily located in the urinary bladder. Leiomyosarcomas are mesenchymal malignant tumours of smooth muscle that most commonly affects gastrointestinal tract, skin and subcutaneous tissue. There are few reports of leiomyosarcoma of the urinary tract in cats and all of them occurred in the bladder.

### Materials and methods

We report a case of a 11 year old male neutered cat that presented at consult with faecal tenesmus, hyporexia and weight loss. Complete blood work, abdominal radiograph and ultrasound were performed and revealed a retroperitoneal mass of unknown origin. A computed tomography was performed to determine the origin and the cat underwent surgery to remove the mass.

### Results

Histopathology was compatible with a fusiform cell sarcoma with morphology of a leiomyosarcoma of urinary origin in the urethra. Two months after surgery the cat developed stranguria and dysuria and a lesion was found at the surgery's site invading the bladder compatible with recurrence and euthanasia was performed.

### Conclusions

The necropsy confirmed a fusiform cell sarcoma in the submucous of the urethra. To the best of our knowledge, this is the first case of primary urethral leiomyosarcoma in the cat and should be included in the differential diagnosis of feline urethral neoplasia.

# Circulating cell free DNA (cfDNA) reveals hidden illnesses in dogs

Milja Tikkanen <sup>1</sup>, Emmi Hurskainen <sup>1</sup>, Petra Jaakonsaari <sup>1</sup>, William von der Pahlen <sup>1</sup>, Hannes Lohi <sup>1, 2</sup>, Juha Kere <sup>1, 3</sup>, Gugan Eswaran <sup>1, 2</sup>, <u>Katja Kivinen</u> <sup>1</sup>

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### Introduction

Circulating cell free DNA (cfDNA) is a promising liquid biopsy analyte for detecting pathological processes before the onset of clinical signs of a disease including cancer. Our findings highlight the utility of cfDNA testing in measuring canine health and monitoring disease treatment success.

# Materials and methods

>3,000 dogs (2,314 presumed healthy; 421 with cancer diagnosis; and 595 with non-cancer diagnosis) were recruited with informed owner consent. An in-house workflow was developed to measure cfDNA from 1ml EDTA plasma reliably and reproducibly. Internal controls and breed-specific reference ranges were generated to improve the test performance further.

# Results

cfDNA concentration correlated with the severity of the underlying pathological process, with highest values seen in systemic cancers. Inflammatory diseases and localised cancers, most notably mast cell tumours (MCT), were seen in the lower end of the spectrum. The effect of pathological processes on cfDNA concentration was cumulative. Serial testing was found to be especially valuable in distinguishing cancers from e.g. inflammatory or chronic diseases, and in monitoring treatment efficiency and detecting disease recurrence.

### Conclusions

We have developed a fast, affordable, and minimally invasive cfDNA-based test to measure the overall health for all dog breeds. The test has wide usability across many cancers as well as chronic and inflammatory diseases, and can be used as part of a standard blood panel to detect a wide range of illnesses, or as a standalone test to monitor the success of ongoing treatments against a known illness.

# Comparison of three lomustine-based protocols as first rescue therapy in dogs with multicentric large B-cell lymphoma

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### Introduction

Lomustine is commonly used as rescue therapy in canine multicentric large B-cell lymphoma (cMLBCL), but the benefits of combined protocols remain uncertain. This study aimed to compare the tolerability and efficacy of three lomustine-based protocols as first rescue therapy in cMLBCL.

### Materials and methods

CHOP-treated cMLBCL cases confirmed via cytology/histopathology and immunophenotyping, first rescued with lomustine-based protocols, were retrospectively selected. Protocols included lomustine and prednisone (LP) alone, or with vincristine (LOP) or L-asparaginase (LAP). Data collected included signalment, staging, drug dosages, adverse events (AEs; VCOG-CTCAEv2), response (cRECISTv1.0) and progression-free survival (PFS). Kaplan-Meier and Log-rank tests assessed PFS, while Pearson's Chisquared and Kruskal-Wallis tests compared response and toxicity.

### Results

Sixty-eight dogs (median age 8 years, weight 23kg) were included (LP=20, LOP=18, LAP=30; Stage III-IV=66, Stage V=2; substage a=45, b=23). Total AEs significantly differed (p=0.0223; LP=23, LOP=29, LAP=100). Neutropenia was the most frequent AE (LP=14, LOP=15, LAP=50), mostly grade I/II (LP=9, LOP=10, LAP=25). ALT elevation differed significantly (p=0.0096; LP=4, LOP=8, LAP=41). Overall response rate and median PFS were LP=25% (CR=5%, n=1) and 31 days (CI95% 21-41); LOP=33.3% (CR=22.2%, n=4) and 43 days (CI95% 42-73); and LAP=60% (CR=50%, n=15) and 65 days (CI95% 43-133). CR rate (p=0.0015) and PFS (LAP vs. LOP p=0.0053; LOP vs. LP p=0.0038; LAP vs. LP p

### Conclusions

In this cohort, LAP and LOP improved PFS compared to LP, with L-asparaginase addition achieving the best response and duration, despite increased but tolerable toxicity.

# Extragenital Canine Transmissible Venereal Tumors in 18 cases in India.

Noopur Desai, Swapna Pendse, Najamu Saqib Regoo

The Cancer Vet

### Introduction

There is limited data about various presentations, behavior and response rate for Extragenital Canine Transmissible Venereal Tumor (ECTVT). The aim of this study was to retrospectively evaluate a subset of dogs in India diagnosed with ECTVT for clinical signs, cytopathology and treatment response. ?

### Materials and methods

Data collected for 18 cases included signalment, age, tumor location, cytopathological diagnosis, dose rate and number of chemotherapy doses required for complete clinical remission (CR). Cytologic diagnosis was further characterized as plasmacytoid, lymphoid or mixed. Vincristine chemotherapy was used as the first line of treatment with addition of Doxorubicin for non-responders.??

# Results

Cases comprised of 12 males and 6 females, median age and weight of 4.5 years and 13 kgs respectively. There were 8 nasal, 4 cutaneous, 2 oral, 2 oronasal, 1 mandibular lymph node and 1 multicentric ECTVT. (2/18)11.1% of the dogs had concurrent genital involvement. Clinical signs included nasal discharge, epistaxis, facial deformity, cutaneous, subcutaneous, oral masses that often ulcerated. Cytologic classification of ECTVT was done in 14 cases where 10 were plasmacytoid, 4? were lymphocytoid. Vincristine monotherapy was used at a weekly dosage of 0.5-0.7mg/m2. CR was achieved in 17 of 18 dogs (94.4%) with Vincristine alone, 1 case required an additional dose of Doxorubicin to achieve a CR. On an average, 4 doses of Vincristine were required to achieve a CR.

### Conclusions

CTVT is an important differential for dogs with extragenital tumors in endemic areas. Response rate and number of chemotherapy doses required are like those previously reported for genital CTVT.

# Feline and canine carcinomas of the nasal cavity

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# Introduction

Carcinomas of the nasal cavity/sinus are rare in cats and dogs. Histopathological subtypes include adenocarcinomas (CA), squamous cell carcinomas (SCC), transitional cell carcinomas (TCC), and anaplastic carcinomas (AC). This study aimed to give an overview of the frequency of feline and canine nasal carcinoma subtypes and to evaluate the data of signalment.

### Materials and methods

The histopathological samples of the nasal cavity/sinus mucosa from 130 dogs and 114 cats submitted to Laboklin GmbH & Co. KG (2017-2023) with a diagnosis of carcinoma and complete signalment data were included. Samples from the nasal planum or unclear location were excluded.

# Results

The sample size ranged from 0.1-1.5 cm (median 0.4) in cats and 0.1-6.5 cm (median 0.5) in dogs. Cats were 2-22 years old (median 13) and dogs 3-16 (median 11). In both species, more male than female animals suffered from nasal carcinomas (70.0% dogs, 59.6% cats). Most feline samples derived from Domestic Shorthair cats (84.2%). Mongrels (n=43), Labrador (n=14), and Golden (n=11) retrievers were the most common canine breeds. Feline carcinomas were classified as CA (81.6%), SCC (9.6%), and AC (8.8%). Canine carcinomas were CA (50.0%), SCC (26.2%), TCC (15.4%), and AC (8.5%). Interestingly, retriever breeds had 72.0% SCC, 16.0% AC, 8.0% CA, and 4.0% TCC. Retrievers suffering from SCC were male in 88.9% of the cases.

### Conclusions

The number of male retrievers with nasal carcinomas, especially SCC, was high. As prognosis varies between histological subtypes, the more aggressive SCC should be considered in nasal masses, especially in retrievers, and histopathological investigation is recommended.

### Radiomics and Comparative Neuroimaging of Canine Gliomas and Human Glioblastomas: A Step Towards Precision Medicine

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### Introduction

Gliomas are primary CNS tumors that significantly affect the quality of life in both dogs and humans. Human glioblastomas are the most aggressive subtype, with a median survival of 15 months post-diagnosis. Brachycephalic dogs are predisposed to gliomas, sharing biological characteristics with human glioblastomas. This study investigated the use of radiomics on T2-FLAIR MRI to characterize tumor and non-tumor tissues, aiming to develop imaging biomarkers for glioma diagnosis and prognosis.

### Materials and methods

MRI scans of canine gliomas and human glioblastomas were segmented to define Regions of Interest (ROIs). Radiomic features, including texture, shape, and intensity, were extracted and analyzed using statistical tests, ANOVA, and ROC curves. Features with an area under the curve (AUC) above 80%, such as "jointaverage" and "autocorrelation," were emphasized.

### Results

Volumetric analysis revealed significant differences in volume distribution between groups (p < 0.001). Selected radiomic features effectively differentiated tissue types, with ROC curves showing AUC values exceeding 80% (p < 0.001). The SVM model achieved an 80.33% classification accuracy.

#### Conclusions

Radiomic features captured heterogeneity patterns reflecting glioma aggressiveness and biological complexity. This supports the use of canine gliomas as translational models for human glioblastomas, contributing to precision medicine. Limitations include the small sample size and need for further validation in diverse populations. Radiomics demonstrated potential in characterizing canine and human gliomas. These imaging biomarkers lay the groundwork for non-invasive diagnostics and comparative approaches, advancing precision medicine.

### Evaluation of thymidine kinase-1 activity in serum and body cavity fluids of horses affected by lymphoma, inflammatory bowel disease and other non-inflammatory gastrointestinal conditions

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# Introduction

Serum thymidine kinase-1 activity (TK1S) is a tumor marker with variable accuracy, while TK1 activity in peritoneal/pleural fluid (TK1PF) remains unestablished in horses.

# Materials and methods

TK1S and TK1PF were measured (chemiluminescent immunoassay) in horses with lymphoma, inflammatory bowel disease (IBD) and other non-inflammatory gastrointestinal disorders (control). Wilcoxon test compared TK1S and TK1PF, while Spearman's rho (?) assessed correlation. Kruskal-Wallis test examined group differences. Data were presented as median and interquartile range. Significance was set at p<0.05.

# Results

There were 10 horses with lymphoma, 8 with IBD and 11 controls. TK1PF (3.52; 1.18-14.15 U/L) was significantly higher (p=0.001) than TK1S (0.69; 0.49-1.89 U/L). There was a moderate correlation between both results (?=0.42, p=0.03). Significant differences were found in TK1S between groups (p=0.02), but not in TK1PF (p=0.35). TK1S in horses with lymphoma (3.45; 0.65-8.16 U/L) was significantly higher (p=0.02) than in controls (0.49; 0.49-0.75 U/L), but not significantly higher than in IBD (0.67; 0.49-1.52 U/L).

# Conclusions

The measurement of TK1PF can be routinely performed on peritoneal or pleural fluid. Notably, TK1PF was significantly higher than TK1S in most horses with lymphoma, although an increase was also observed in a few horses with IBD. The small sample size could have prevented detection of differences in TK1PF between groups. In addition, inflammation associated with gastrointestinal disease could potentially increase both TK1S and TK1PF.Reference ranges for TK1PF in horses should be evaluated. Further studies are needed to assess its usefulness in lymphoma diagnostics.

# Morphological Characterization of Organoids Derived from Canine Mastocytomas: Insights into Tumor Architecture

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### Introduction

Canine mastocytomas are among the most prevalent cutaneous tumors in dogs, providing an important model for studying mast cell tumor biology. Organoid technology is emerging as a revolutionary tool in cancer research, offering three-dimensional in vitro models that replicate the native tumor environment. This study focuses on the morphological characterization of organoids derived from mastocytomas, providing novel insights into their cellular architecture and tumor heterogeneity.

### Materials and methods

Organoids were cultured from tissue samples obtained from three canine mastocytomas confirmed by cytology and histopathology. The tissues were enzymatically and mechanically dissociated, followed by embedding in a three-dimensional Matrigel® matrix. Organoids were maintained in a specialized medium composed of Advanced DMEM/F12 supplemented with key growth factors (Wnt-CM, R-spondin, FGF, NOG, EGF), Rock inhibitor, and antibiotics. Morphological analyses were performed using light microscopy, allowing detailed visualization of structural features.

### Results

Microscopic evaluation revealed organoids exhibiting well-defined spheroidal structures with compact cellular aggregates. These organoids ranged from 30–150 µm in diameter, showing distinct peripheral zones of tightly packed cells indicative of mitotic activity, while central regions displayed loose cellular aggregation suggestive of hypoxic or necrotic cores. Intercellular spaces and vacuolated areas contributed to the heterogeneity of their morphology. In some cells, granulated cytoplasm was observed, consistent with mast cell characteristics and indicative of retained tumor-specific features.

#### Conclusions

This study provides the first detailed morphological description of organoids derived from canine mastocytomas. These findings support future investigations, including full molecular and immunohistochemical characterization, to enhance the understanding of tumor biology and advance veterinary oncology.

# Characterization of tumour epidemics in reptiles from the Budapest Zoo

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### Introduction

Cancer in zoo animals is a subject that is gaining relevance along the years. The aim of this study was to characterize tumor epidemics in the population of reptiles at Budapest Zoo in the last two decades.

### Materials and methods

Medical records from reptiles kept in Budapest Zoo and Botanical Garden between 2006 and 2024 were analysed. All the histologic diagnosis were made after samples performed at the time of necropsy. Data from animal species, age, tumor location and year of diagnosis was recorded and analysed.

### Results

Thirty tree cases of reptiles affected by tumors were described in the last 19 years. For all cases clinical data and tumor histology were available. Snakes were the most affected contributiong for 60% of cases. Lizards were the second most affected species with 37% of cases. Adenocarcinomas were the most common reported malignant tumors representing 23% of the total tumor burden. Small reptiles with less than 1 Kg of body weight were the most affected (63%). Cancer records increased 100% between 2023 and 2024.

#### Conclusions

This study contributes to understand cancer epidemic in reptiles kept in captivity, highlighting that snakes and reptiles with less than 1 kg body weight can be at major risk to develop malignant tumors, namely adenocarcinomas. It would be important to perform a prospective study to understand if captivity's environmental conditions can increase cancer risk in reptiles.

# Cell-free DNA as a biomarker for electrochemotherapy and IL-12 gene electrotransfer treatment response in dogs

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### Introduction

Electrochemotherapy (ECT) with interleukin-12 gene electrotransfer (IL-12 GET) has shown local and systemic effects in treating canine mast cell tumours (MCT). To predict and evaluate the treatment response noninvasively (without tissue biopsies), liquid biopsy, such as cell-free DNA (cfDNA) from the blood, presents a promising diagnostic strategy. Therefore, this study aimed to evaluate cfDNA values from the blood of dogs with MCT treated with ECT + IL-12 GET to correlate the results with treatment response.

### Materials and methods

The study included 15 dogs with MCT (FNAB or histology) treated with the ECT + IL-12 GET. Blood plasma was collected before and 8 weeks after the treatment, and the response was evaluated using RECIST criteria. Next, cfDNA was isolated from plasma, and its concentration and fragment size distribution were analyzed.

### Results

The results of this study indicated that 12 dogs achieved objective responses: complete or partial response (CR, PR); 1 had stable disease (SD), and 2 had progressive disease (PD). Furthermore, 8 weeks after treatment, the mean cfDNA values for CR dogs were the lowest at 1.97 ng/µl, while PD dogs had the highest values at 43.65 ng/µl. The PR mean was 7.66 ng/µl, and SD had an average of 6.28 ng/µl.

### Conclusions

The results of this study suggest that cfDNA could be a promising biomarker for tracking tumour progression, predicting treatment response, and guiding clinical decisions. However, these findings should be interpreted cautiously, as larger studies with diverse tumour types and longer follow-ups are needed to confirm the results.

# Prognostic value of serum Albumin and Albumin:Globulin ratio in dogs with Diffuse Large B-cell Lymphoma

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### Introduction

Cost-effective prognostic markers are crucial for optimizing DLBCL treatment in dogs. This study evaluated pre-treatment serum albumin and albumin:globulin ratio as prognostic indicators in dogs with DLBCL treated with CHOP protocol.

### Materials and methods

Fifty-nine dogs with confirmed DLBCL were enrolled. The association between pre-treatment albumin and albumin:globulin ratio (AGR) with time to progression (TTP) and overall survival (OS) was analyzed. Time-to-event endpoints were assessed at 180 and 365 days. Receiver operating characteristic (ROC) curve analysis determined optimal cut-off values.

### Results

The median OS and TTP were 206 and 120 days, respectively. ROC curve analysis revealed that: at 180 days, for TTP, albumin showed good discrimination (AUC 0.805, p

### Conclusions

Pre-treatment albumin and AGR are valuable, readily available prognostic indicators for dogs with DLBCL treated with CHOP. These parameters can aid in risk stratification and affect treatment decisions. Further research in larger cohorts is warranted to validate these findings. The low cost and ease of measurement make these markers valuable tools in veterinary oncology.

# Retrospective Evaluation of Chemotherapy-Associated Adverse Events from a Single Institution

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### Introduction

Cytotoxic chemotherapy is well-tolerated by most dogs; however, serious and life-threatening adverse events occur in a subset of dogs, yet few evidence-based reports exist to quantify this. The aim of this project was to identify the frequency of chemotherapy adverse events (AE) resulting in hospitalization and death and examine which chemotherapy agents were most frequently associated.

# Materials and methods

A pharmacy search from January 1, 2022 to April 1, 2024 was performed to identify dogs that had been treated with doxorubicin, carboplatin, vincristine, vinblastine, cyclophosphamide, lomustine, mitoxantrone and rabacfosadine. Dogs were included in the study if the drug had been administered as a single-agent and adequate follow-up existed to assess acute AE. Only the first instance that the drug was administered was included in the analysis. Severity of AE was grouped into four categories: no dose reduction/delay needed, dose delay or dose reduction for future treatments required, hospitalization needed, and death.

# Results

Seven-hundred seventy-nine single-agent chemotherapy administrations to 452 dogs were evaluated. Overall, AE were absent to mild for 578 (74%) treatments, 158 (20%) treatments resulted in dose delays or reductions, 32 (4.1%) treatments required hospitalization to manage, and 11 (1.4%) dogs died secondary to chemotherapy. Carboplatin, doxorubicin, and vincristine administrations had the highest frequency hospitalization at 39%, 30%, and 19%, respectively. Carboplatin, doxorubicin, and lomustine had the highest frequency of death secondary to treatment at 53%, 16%, and 12%, respectively.

# Conclusions

Chemotherapy is well-tolerated in most dogs, and carboplatin administration was associated with the greatest frequency of hospitalization and death.

# ELECTROCHEMOTHERAPY TREATMENT APPROACH FOR FELINE SQUAMOUS CELL CARCINOMA IN THE HEAD

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### Introduction

Electrochemotherapy (ECT), an approach involving the administration of targeted chemotherapeutic drugs alongside electrical pulse application, has emerged as a promising treatment for feline Squamous cell carcinoma (SCC). This retrospective study aimed to assess the effectiveness and safety of ECT, while identifying potential prognostic factors, in cats with SCC in the head.

### Materials and methods

To be eligible, cats must have a confirmed histopathological or cytological diagnosis of SCC in the head, staged according to WHO guidelines, have undergone at least one ECT treatment (Electrovet EZ) with intravenous bleomycin, and have at least one year of follow-up. Clinical response was evaluated (RECIST guidelines) and the treatment side effects were recorded at follow-up (VCOG?CTCAE v2). Endpoint analysis involved evaluating the overall response rate (RR), progression-free survival (PFS), disease-free interval (DFI), and overall survival (OS).

### Results

Eighty-six cats were included. In 71 (82.56%) the tumor was in the nasal planum, 15 (17.44%) pinna, and 10 (11,63%) eyelid. The RR was 79,07%. Tumor size Tis, T1, and T2 had a complete response (CR) of 67.65%, while T3 and T4 had 38.89%. The median of DFI was 398 days, the median of PFS was 49 days, and the median of OS was 807 days. Recurrence occurred in 37% of the cats with CR. Thirty-eight survived until the end of the study, and 4 cats were lost to follow-up.

### Conclusions

Accompanied by mild to moderate side effects in 68.8% of the animals, ECT proves efficacious and safe in the treatment of small SCC, offering a viable alternative to surgery or radiotherapy.

# Combined conservative surgical approach with electrochemotherapy in four canine patients diagnosed with nasal planum squamous cell carcinoma

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### Introduction

The role of electrochemotherapy (ECT) in managing canine nasal planum squamous cell carcinoma is still to be evaluated either as single or combined therapy. Herein we described a case series were a combined approach of conservative surgery and electrochemotherapy was used to treat nasal planum squamous cell carcinomas (nSCC).

### Materials and methods

The clinical study was conducted from 2022 to 2024.All the animals had previously a diagnosis of nSCC. Staging was performed using computed tomography and lymphnode cytology. Surgery consisted of a marginal removal of the tumor. ECT was performed intrasurgically on the tumor bed: bleomycin was administered intravenously (15 mg/m2) and after 8 minutes, a series of electrical pulses (ELETROvet EZ, Leroy Biotech), were applied. Resected tumors were sent histological margins report.

# Results

All the dogs were males. Mean age was 12 years. All the histological margins were contaminated with tumor. All tumors were staged as T2N0M0. Only 1/4 dogs had recurrence two months after surgery. Post-treatment complications were present in all dogs, sneezing and muco/sanguinolent discharge the most commons. Only one owner was not happy with the cosmetic appearance, due do septal cartilage deformation and that was the dog with recurrence.

# Conclusions

Conservative surgery followed by intra operative ECT revealed a good disease control in 75% of patients with a time to recurrence superior to 1 year in dogs affected by locally invasive nSCC.

# NURSE CASE PRESENTATIONS

# Gold standard care for oncology feline patients: Approaches and best practices

# Jodie Wilcox, Rebecca Rudolf

### **Biography**



**Jodie Willcox** started working at a local mixed practice in Cheshire before qualifying as a RVN in 2013 before moving to ChesterGates referral hospital in 2014. In 2016 she joined Northwest Veterinary Specialists, where she is head nurse of oncology, medicine and pharmacy. She gained her Advanced Diploma (Small Animal), and HE diploma in Clinical Veterinary Nursing in 2019, which is also around the time she found her love for oncology nursing. Ensuring fear free, gold standard patient care and supporting patient carers is what Jodie feels most passionate about. At home she has a 14year old pug called Doug.



**Rebecca Rudolf** is a Registered Veterinary Nurse (RVN) who has been qualified since 2013. She joined Northwest Veterinary Specialists in 2014, where she has gained extensive experience across a range of specialist disciplines. Her passion for oncology led her to transition into the hospital's busy oncology department, where she plays a key role within the team. Since then, Rebecca has developed a particular interest in creating a low-stress, fear-free environment for oncology patients. She is dedicated to ensuring that each patient visit is as comfortable and positive as possible, consistently delivering high-quality, patient-centred care. Rebecca is also a proud dog mum to two Labradors Oscar and Bruce.

### Abstract Overview

The presentation will explore the gold standard of care for feline oncology patients, focusing on the knowledge and understanding of best practices in an ISFM gold accredited veterinary hospital. Attendees will gain insight into the care for feline patients from admittance to discharge, including our feline chemotherapy protocols to ensure a smooth and stress-free environment for our patients.

A feline oncology patient undergoing treatment at our ISFM Gold Accredited veterinary hospital receives care tailored to both their clinical needs and emotional wellbeing. From the point of diagnosis through ongoing treatment and follow-up, every aspect of the patient journey is guided by feline-friendly principles that aim to reduce stress, support recovery, and ensure the best possible quality of life.

### **Treatment Summary**

Upon presentation, patients usually undergo a diagnostic workup including blood analysis, diagnostic imaging, and cytology or histopathology to confirm the type and stage of cancer (if not already determined). A personalised treatment plan is then developed, often involving chemotherapy protocols such as COP or single-agent therapies, depending on the diagnosis and patient tolerance.

Follow-up visits are scheduled to assess response to treatment through physical examination, repeat bloodwork, and imaging where needed.

Our patients receive not only advanced medical treatment but also compassionate support in a setting designed to respect their natural behaviours and reduce anxiety.

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# **Nursing Interventions**

Throughout the course of treatment, the nursing team plays a central role in the administration of the chemotherapy, following cytotoxic handling protocols to protect both the patient and the team.

Each chemotherapy session is carefully planned to minimise stress:

- **Pre-treatment medications**, including anti-nausea drugs and gabapentin, are prescribed by the MRCVS when appropriate to reduce anxiety, minimise nausea, and promote comfort and tolerance to treatment.
- Having a dedicated feline-only waiting area and consult room where feline patients and their owners can relax in a calm, quiet environment prior to the admit
- Using a cat transportation device to facilitate stress free movement around the hospital
- Admitting patients directly to a quiet, feline-only ward equipped with pheromone diffusers, soft bedding, hiding places, and low lighting to promote a calm and secure environment.
- Using pheromone-infused bedding and kennel covers to further aid in reducing stress and support a relaxed, feline-friendly atmosphere.
- **Designating a feline-only treatment area for procedures** including physical examination, blood collection and chemotherapy administration
- Applying topical anaesthetic creams and vapo-coolant sprays to minimise discomfort during intravenous catheter placement and blood sampling
- Always using feline-friendly handling techniques, minimising restraint and allowing the cat to remain in their carrier or hiding space when possible.
- Utilising nutraceutical calming treats, such as "Feliway Happy Snacks," to reduce stress and facilitate cooperative behaviour during examinations and treatment procedures.
- Approaching all interactions slowly and gently, allowing the patient time to acclimate to each step of care.

# **Key Learning Points**

- Each feline oncology patient should be treated as an individual, with personalised care plans that consider their unique medical and emotional needs.
- **Incorporating multimodal and multidisciplinary stress-reduction strategies** is essential to improve treatment tolerance and overall wellbeing in feline oncology patients.
- **Developing practical, hands-on skills in feline-friendly techniques** ensures the consistent delivery of high-quality oncology care and contributes significantly to patient comfort and safety

### **Electrochemotherapy aftercare**

# Daniela Andrade

# **Biography**



**Daniela Andrade** graduated as a Veterinary Nurse in 2015 in Portugal where she worked for a year in a small animal practice. In 2017 she came to the UK and started her first job as an RVN at a small animal practice, after a year Daniela moved into a small animal hospital and finally in 2019 she started her position as a nurse across all areas at Davies Veterinary Specialists. In 2021 she joined the Oncology team, where she developed her interest in oncological patient care. Daniela is currently finishing her certificate in medical nursing and would like to further specialise in oncology.

### Abstract

This case refers to an, histologically diagnosed, angiomatosis\hemangiosarcoma with low mitotic index on the palmar aspect of the left hind limb of a 13-year-old male neutered Border Terrier. The patient presented with chronic bleeding and recurrent infections of a 1.6cm x 2cm mass infiltrating on the main pad. Staging with CT scan of the chest and abdomen at the time of presentation did not show any other lesions. Surgical options for this case were considered and included total amputation of the limb or marginal removal of the mass through partial removal of the pad, the later having the potential to cause long term lameness. In case of marginal removal, electrochemotherapy could have been used as an adjuvant treatment after surgery. However, these options were declined by the owner and instead it was agreed to treat with electrochemotherapy alone. A single treatment with intravenous Bleomycin followed by reversible electrochemotherapy of the entire paw, owing to the risk of infiltration, was performed. Due to the high irrigation of this tumour, a bandage was applied post-treatment and the owner advised to go back to the referring veterinary practice for regular bandage changes. When the patient presented for a re-check two weeks later, the wound dressing applied had adhered to the wound, and as a result, most of the metatarsal pad was ulcerated with a small 5mm necrotic area. In addition, bleeding and granulation were also noted. The hair from the palmar aspect of the foot was clipped and the necrotic area of the pad debrided, the wound was then flushed with saline and the foot bandaged with a foam dressing (e.g. Allevyn®), as the contact layer, and a standard threelayer bandage. A further two weeks down the line, the treated area showed marked improvement with the previously necrotic area almost covered by scar tissue. The tumour showed a partial remission. At the re-check two months post the initial electrochemotherapy treatment the area was completely healed with only mild alopecia persisting. The owner was advised that the remaining changes could be secondary to the treatment with electrochemotherapy, but persistence of the tumour could not be ruled out. Repeated imaging and treatment with conventional chemotherapy (Doxorubicin) were offered and declined by the owner, and so it was decided to monitor the area for further changes. Nine months after the initial electrochemotherapy treatment this patient continues to do well with no sign of recurrence of his previously diagnosed hemangiosarcoma/ angiomatosis.

### Learning Objectives for this Session

- (i) Electrochemotherapy can be a valuable treatment option in the gross disease setting, particularly in vascular tumours.
- (ii) It's important to consider the damage this treatment can cause to the tumour and surrounding tissues and plan aftercare for these patients.
- (iii) Veterinary nurses can be involved, not only in the electrochemotherapy procedure but also, in the initial discussion of the case and aftercare of these patients.

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# Behavioural challenges (the perfect chemotherapy patient)

# Abi Bennet (RVN, CertVNECC)

### **Biography**



I qualified in 2017 through Abbeydale college whist working at Zetland Vets in Bristol, UK. In 2019 I joined Rowe Referrals, gained the VetsNow ECC Cert, then started working in Medicine before transitioning nearly 2 years ago into Oncology. I am looking to further my education and training with an oncology nursing certificate.

The favourite parts of my job? Being able to advocate for the patients and making the last part of their lives as comfortable and dignified as possible; plus building relationships with the patients and clients.

Interesting fact, not much to report on that front  $\mathfrak{S}$ ! Have a 3yr old boy called Arthur and a very messed up Border terrier... (staff pets  $\mathfrak{S}$ )

### Abstract

Roo presented to the clinic as a surgical oncology case – he was diagnosed with a forelimb osteosarcoma. His behaviour set us many challenges that we had not come across before.

Roo was a rescue dog from Portugal; he had a brief history (4 years) of behavioral challenges at the vets. He had previously been treated as an outpatient when he should have been treated in the clinic due to his anxieties.

Challenges with the owners accepting that Roo needed medical help with these problems, getting them on board started off as a challenge they did not like the sedative state he was in and wanted to reduce medications causing him to pace and jump around post operatively. Causing delays in wound healing and then us starting his chemotherapy.

The team had a sit down before the surgery to discuss both the anesthesia/ analgesia plan and the ethics of the procedure – ultimately it was decided to go ahead.

Pre clinic sedation was given at home; the diary was altered to reduce any extra stress that Roo may meet.

Open, honest and frank conversations were had between the team and the client to make sure that throughout his treatment he was being advocated for and that we had the right interests at the forefront of his treatment.

Our chemotherapy protocol had to be altered; it initially suggested that any 'behavioral' patient was not suitable for treatment. We challenged that with the IVC board – we believe that with the right medications and owners, these patients deserve a chance.

The RVN struggled to eliminate all of the external triggers for Roo, there were days where the lab were delayed meaning that Roo either waited for periods of time in the car or went off and had a walk – by the time he was back in the clinic, his peak sedation levels were settling meaning we were having to give increased doses intramuscularly.

Roo became attached to one RVN and some days due to annual leave or sickness that RVN was not around – causing extra stress for the patient.

What was learnt – every patient is different, what is a trigger for one may not be for the other. It is ok to send the patient away and try again another day – pushing through the stress is not always the right thing to do.

Patience was a significant factor to learn for all the team, these challenging cases force us back to the patient – take the extra time, work at a pace the patient is comfortable with.

Trouble shoot before the patient comes into the clinic, 'risk assess' the environment – reduce or remove any factors that may affect the patient in a negative way.

Spend time taking a history from the client – what are their favourite snacks – what do they like and do not like. What helps to settle them.

We as a rule do not do anything in the kennels, these are their safe spaces and are always pre sprayed with Adaptil and pet remedy or Feliway.

Speak up for your patient – be their voice as they do not have one.

# The veterinary nurse's intervention in nasal squamous cell carcinoma in cats

### Ana Seco

# **Biography**



Graduated in Veterinary Nursing from Escola Superior Agrária de Viseu (2008). Holds a postgraduate diploma in Practical Techniques in Veterinary Practice (2012, Improve International) with a Nurse Certificate in Practical Tecniques by ESVPS and a Master's degree in Marketing from the University of Aveiro (2018). Currently pursuing a PhD in One Health at the University of Trás-os-Montes and Alto Douro (since 2024, UTAD). Working as a veterinary nurse at Clínica Veterinária Planeta

Animal since 2010, and since 2022 also responsible for marketing, with a special focus on client communication. Founder of the Vet Nurse Daily community (2013), co-creator of the Vet Nurse FM podcast (2020), and Vice-President of the Portuguese Veterinary Nurses Association. A professional path dedicated to clinical care, education, and strategic communication, promoting an integrated and current approach to veterinary nursing.

### Abstract

Cutaneous squamous cell carcinoma (cSCC) is the most common skin cancer in Portuguese cats, particularly affecting older, light-colored, short-haired animals due to their increased exposure to ultraviolet (UV) light. Typically arising in sun-exposed areas such as the nasal planum, ears, and eyelids, cSCC lesions are often first noticed by owners as non-healing wounds. Although these tumors metastasize slowly, they are locally aggressive and can significantly compromise an animal's quality of life if not detected and treated early.

This case involved a 7-year-old European Shorthair cat, positive for feline immunodeficiency virus (FIV), presenting with a year-old ulcerated lesion on the nasal planum. The lesion had proven resistant to prior cryotherapy and was suspected to be cSCC following inconclusive cytology indicating cellular atypia. Due to the lesion's severity and the limitations of surgical intervention—including the inability to achieve clean margins and the cosmetic concerns of nosectomy—electrochemotherapy (ECT) was chosen as the preferred treatment.

The cat underwent one ECT session with intratumoral administration of cisplatin. Posttreatment care included a multimodal approach to ensure the cat's comfort and recovery. This involved an 8-day course of Robenacoxib (6 mg), routine temperature monitoring, and strict nutritional oversight due to potential anosmia post-treatment. Additionally, an Elizabethan collar was used to prevent self-trauma, and the cat attended weekly follow-ups to assess lesion response. Although partial healing was achieved, a second ECT session was recommended to further reduce the remaining ulceration and improve outcomes.

ECT has been shown to be effective and well tolerated in cats with advanced cSCC, offering a non-invasive alternative with minimal side effects and a meaningful extension of both quality and length of life. At Planeta Animal Veterinary Clinic, over 40 ECT treatments have confirmed the procedure's efficacy in managing facial cSCC cases, particularly where surgery is not feasible.

Veterinary nurses played an essential role throughout the treatment process—monitoring the animal's condition, guiding the owner through at-home care, and supporting both the pet and caregiver emotionally. More broadly, veterinary nurses are pivotal in cSCC prevention and early detection. Their responsibilities extend to educating owners about risk factors, sun protection, and recognizing early symptoms. By organizing informational events, segmenting at-risk patient databases, and conducting preventive consultations, nurses can directly impact outcomes.

This case underscores the importance of empowering veterinary nurses not just in treatment, but also in proactive client education. With the rise of millennial pet owners who value collaborative care, veterinary teams must embrace communication strategies that resonate with today's clientele. Encouraging early screenings and consistent owner engagement can drastically improve prognosis for feline cSCC cases, preventing suffering and reducing the need for invasive treatments or premature euthanasia.

# 3 key learning points from this case:

- 1. Identify the signs and risk factors of squamous cell carcinoma (cSCC) in cats;
- 2. Understand how the veterinary nurse can help prevent cSCC by educating pet owners;
- 3. Know the nursing care before, during and after electrochemotherapy (ECT).

# Offering support during a patient's twilight weeks

# Carrie Harvey, RVN

# **Biography**



I qualified as a veterinary nurse in 2013, and have been working in oncology, at the Royal Veterianrey College for the last 10 years.

My passion lies in palliative care, in supporting both the patient and their family to ensure a dignified death. With the help of my amazing colleagues, we are currently setting up a palliative care clinic within our department. I hope in the future to roll it out across the other services to create a palliative care team for the entire hospital.

At home I am a busy mum to two children and three cats. In my spare

time I enjoy cycling through the countrysides, reading crime fiction and cooking for my friends and family.

### Abstract

This case study follows Olive, a 13 year old, FN, English bulldog, who was diagnosed with cutaneous epitheliotropic lymphoma in July 2024. In December Olives owners opted for palliative care when treatment with isotretinoin and masitinib was unsuccessful due to progression of the cancer. Olives lymphoma was very diffuse with large regions of erythema and nodular lesions across the ventral thorax, abdomen, medial thighs, peri-anus and on her face. Her main concerns were pain, pruritus, mobility and breakdown of the skin barrier, leading to infection.

This presentation will look into how, as nurses, we supported not only Olives physical and medical needs, but also the emotional needs of the owners during such a difficult time. Building a trusting rapport and having open and clear communication with the owners ensured Olive had a good quality of life with minimal suffering up until her peaceful and dignified euthanasia. It also allowed Olives owners to have time to come to terms with her prognosis and prepare for the emotional journey that comes with death and grief.

### Key Learning objectives

- How nurses can help support patients that have advanced cancer to prevent suffering and ensure a good quality of life is maintained.
- Using quality of life tools to help assess the right support needed for the palliative patient and to decide when the time is right for euthanasia.
- Having honest, open and empathetic communication to help owners come to terms with their pets prognosis and euthanasia.



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