



Intérêt de la radiothérapie et de la chimiothérapie dans le traitement des tumeurs intracrâniennes des carnivores domestiques

Pauline de Fornel-Thibaud



Traitement des
tumeurs intra-
crâniennes

Introduction

Epidémiologie

Contexte épidémiologique

• Incidence :

14,5 /100 000 chiens et 3,5 /100 000 chats

2,8 % des chiens et 2,2% des chats

Contexte épidémiologique

•!Types tumoraux dans l'espèce canine :

-!primitives :

-!méningiomes (45%)

-!tumeurs gliales : astrocytomes (17%)

oligodendrogliomes (14%)

-!autres tumeurs neuro-épithéliales

-!secondaires :

-!métastases (hémangiosarcome)

-!tumeurs hypophysaires

-!lympho

J. Vet Intern. Med. 2009;23:618-621

Canine Intracranial Primary Neoplasia: 173 Cases (1986–2003)

Jessica M. Snyder, Frances S. Shofer, Thomas J. Van Winkle, and Christine Massicotte

Contexte épidémiologique

•!Types tumoraux dans l'espèce féline :

-!primitives :

-!méningiomes (57%)

- tumeurs gliales : astrocytomes, oligodendrogliomes (7%)

-!autres tumeurs gliales

-!secondaires :

-!métastases (hémangiosarcome) (5%)

-!tumeurs hypophysaires (9%)

-!lymphomes (14%)

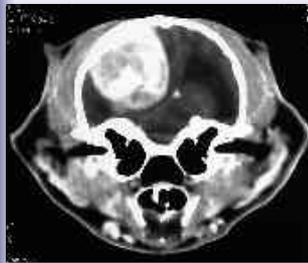
J. Vet Intern. Med. 2002;16:279-284

Feline Intracranial Neoplasia: Retrospective Review of 160 Cases (1985–2001)

Mark T. Truex, Charles H. Vite, Thomas J. Van Winkle, Alisa L. Newton, Deana Thelmer, Nancy Dayzel-Hart, Amy S. Kupatkin, Frances S. Shofer and Sheldon A. Steinberg

Contexte épidémiologique

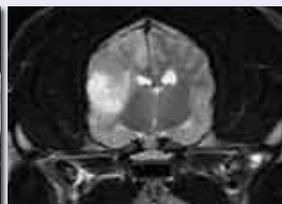
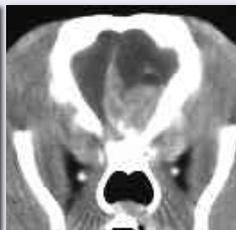
- !Types tumoraux dans l'espèce féline :
- !primitives :
 - !méningiomes (57%)



Traitement chirurgical
Médiane de survie : 21 mois
Nbreux chats vivants après 2 ans

Modalités diagnostiques

- !Examens d'imagerie médicale



Modalités diagnostiques

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- ! Examens d'imagerie médicale
- ! Biopsies et examens anatomo-pathologiques

Stereotactic CT-guided brain biopsy in the dog

F. Meiswinkel, S. Boer, P. Dechant, J. Durkin, J. De Groot, C. Looze, M.A. Oude-van-der-Jonckheere

Journal of Small Animal Clinical Practice 2007



J. Vet Intern Med 2006;20:669-675

Canine Intracranial Primary Neoplasia: 173 Cases (1986–2003)

Jessica M. Snyder, Frances S. Shofer, Thomas J. Van Winkle, and Christiann Massicotte

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Table 4. Magnetic resonance imaging (MRI) findings in 24 dogs with primary intracranial tumors.

Tumor Type (No. of Cases)	Site (No. of Cases)	Signal Intensity (T1, T2, FLAIR, DWI)	Enhancement (T1 post-contrast)	Peritumoral Edema (T2, FLAIR)	Mass Effect (Midline Shift, Ventricular Compression)	Other Findings
Meningeoma (9)	Cerebral (8), Infratentorial (1)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Chondrosarcoma (3)	Infratentorial (3)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Oligodendroglioma (5)	Infratentorial (5)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Astrocytoma (6)	Infratentorial (5), Infratentorial (1)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Glioblastoma (1)	Infratentorial (1)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Ependymoma (1)	Infratentorial (1)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None
Lymphoma (1)	Infratentorial (1)	Isointense to gray matter (T1), hypointense (T2), hyperintense (FLAIR), variable (DWI)	Heterogeneous (T1), homogeneous (T2), nodular (T1 post-contrast)	Minimal to moderate (T2, FLAIR)	Minimal to moderate (Midline shift, Ventricular compression)	None

Magnetic resonance imaging findings in 40 dogs with histologically confirmed intracranial tumours^{1,2}

Sergio Ródenas^a, Martí Pumarola^a, Lluís Gàitero^a, Àngels Zamora^b, Sònia Añor^{a,*}

^aDepartment of Animal Medicine and Surgery, Veterinary School, Autonomous University of Barcelona, 08193 Bellaterra (Barcelona), Spain
^bMedina Resonancia Magnética, S.A. 08520 Sant Joan Despí (Barcelona), Spain

The Veterinary Journal 187 (2011) 85–91

MAGNETIC RESONANCE IMAGING FEATURES OF CANINE INTRACRANIAL NEOPLASIA

ERIK R. WISNER, PETER J. DICKINSON, ROBERT J. HIGGINS

Although histologic examination following stereotactic or surgical brain biopsy is required for definitive antemortem diagnosis of intracranial neoplasms, these tumors are often associated with magnetic resonance (MR) imaging features that warrant a presumptive or prioritized differential diagnosis. The MR imaging features of common canine central nervous system (CNS), adenohypophysial, and metastatic intracranial neoplasms are reviewed. Characterization of neoplasms by histologic type and biological grade is based on the 2007 World Health Organization classification system for CNS tumors in humans. © 2011 *Veterinary Radiology & Ultrasound*, Vol. 52, No. 1, Suppl. 1, 2011, pp S52–S61.

J Vet Intern Med 2010;24:160–165

Cross-Sectional Imaging Characteristics of Pituitary Adenomas, Invasive Adenomas and Adenocarcinomas in Dogs: 33 Cases (1988–2006)

Rachel E. Pollard, Christopher M. Reilly, Megan R. Uerling, Farica D. Wood, and Edward C. Feldman

Magnetic Resonance Imaging and Histological Classification of Intracranial Meningiomas in 112 Dogs

B.K. Sturges, P.J. Dickinson, A.W. Bollen, P.D. Kobiik, P.H. Kass, G.D. Kortz, K.M. Vernau, M.F. Knipe, R.A. LeCouteur, and R.J. Higgins

Table 3. T2W images: Summary of MRI findings.

Histology	Signal Uniformity		Signal Intensity			Edema		
	homo	hetero	Hyper	Iso	Hypo	Diffuse	Focal	None
Histological grade (n = 112)								
Grade I	44	19	45	16	2	32	27	4
Atypical	48	16	37	11	0	25	20	3
Malignant	1	0	1	0	0	1	1	0
	77	35	83	27	2	58	48	7
Histo subtype								
Grade I tumors (n = 65)								
Meningothelial	27	20	2	18	7	13	14	0
Transitional	25	17	8	20	5	11	11	3
Microcystic	5	2	3	4	1	4	1	0
Panamo	4	3	1	3	0	3	1	0
Angioma	2	2	0	2	0	1	0	1
	44	39	45	16	2	32	27	4

Intérêt pronostique du grade ou du sous type ?

Modalités diagnostiques

- ! Examens d'imagerie médicale
- ! Biopsies et examens anatomo-pathologiques

Options thérapeutiques non chirurgicales

- ! Radiothérapie
- ! Chimiothérapie
- ! Traitement palliatif

Traitement des tumeurs intracraniennes

Informations disponibles dans la littérature...

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Preliminary Study of Lomustine in the Treatment of Intracranial Masses in Dogs Following Localisation by Imaging Techniques.

L.M. Fulton, H.S. Steinberg. Sem. Vet. Med. Surg. 1990. 5(4), 241-245

Diagnostic par imagerie:
3 méningiomes, 2 GBM, 3 astro, 7 ?

J Vet Intern Med 1999;13:408-412

Hypofractionated Radiation Therapy of Brain Masses in Dogs: A Retrospective Analysis of Survival of 83 Cases (1991-1996)

Malcolm J. Brearley, Nick D. Jeffery, Susan M. Phillips, and Ruth Dennis

Diagnostic par imagerie:
Intra-axiales, extra-axiales, hypophysaires

PRIMARY IRRADIATION OF CANINE INTRACRANIAL MASSES

ENRICO P. SPUGNINI DVM, DONALD E. THRALL DVM, PhD, G. SYLVESTER PRICE DVM, PhD, NICHOLAS J. SHARP BVMS, PhD, KAREN MUNANA DVM, RODNEY L. PAGE DVM
Veterinary Radiology & Ultrasound, Vol. 41, No. 4, 2000, pp. 577-581

Diagnostic par imagerie:
22 méningiomes, 4 gliomes, 3 TPC

Chimiothérapie

J Vet Intern Med 2001;15:844-850

Irradiation of Brain Tumors in Dogs with Neurologic Disease

Carla Ribeiro Riley, Andrea Sampson, Melgorata Hiras, and Barbara Knecht-Slater

Diagnostic par imagerie:
Intra-axiales, extra-axiales, hypophysaires

Traitement des tumeurs intracraniennes

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Surgery alone or in combination with radiation therapy for treatment of intracranial meningiomas in dogs: 31 cases (1989-2002)

Todd W. Axlund, DVM, DACVP, Steve E. McGlone, VC, Jennifer N. Smith, DVM, MS, DACVP

Post-opératoire, mégavoltage, photons
28-49 Gy, 4 Gy/séance

J Vet Intern Med 2004;18:460-465

Vascular Endothelial Growth Factor Expression in Canine Intracranial Meningiomas and Association with Patient Survival

Simon R. Platt, Timothy J. Scaris, Vicki Adams, Lara Wiatrowski, Jodi Miller, Filippo Adams, and Sam Long

Post-opératoire, mégavoltage, photons
37 Gy, 5-8 Gy/séance, 3 champs

J Vet Intern Med 1999;13:408-412

Hypofractionated Radiation Therapy of Brain Masses in Dogs: A Retrospective Analysis of Survival of 83 Cases (1991-1996)

Malcolm J. Brearley, Nick D. Jeffery, Susan M. Phillips, and Ruth Dennis

Mégavoltage, cobalt, photons
38 Gy, 5-9 Gy/séance, 3 champs

PRIMARY IRRADIATION OF CANINE INTRACRANIAL MASSES

ENRICO P. SPUGNINI DVM, DONALD E. THRALL DVM, PhD, G. SYLVESTER PRICE DVM, PhD, NICHOLAS J. SHARP BVMS, PhD, KAREN MUNANA DVM, RODNEY L. PAGE DVM
Veterinary Radiology & Ultrasound, Vol. 41, No. 4, 2000, pp. 577-581

Mégavoltage, cobalt, photons
48 Gy, 3Gy/séance, 2 à 4 champs

J Vet Intern Med 2001;15:844-850

Irradiation of Brain Tumors in Dogs with Neurologic Disease

Carla Ribeiro Riley, Andrea Sampson, Melgorata Hiras, and Barbara Knecht-Slater

46 CN : mégavoltage 35-45 Gy; 12 CN : 12-31 MeV e-, 1 à 2 champs
31 CN : photons, 16 MeV e-, 3 à 4 champs; 2 CN : protons et électrons

Traitement des tumeurs intra-crâniennes

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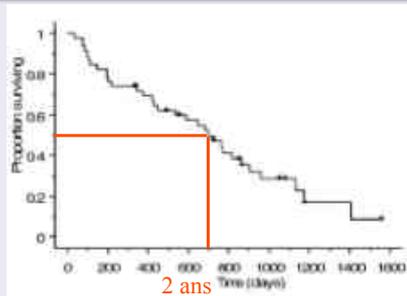
Radiothérapie

Traitement palliatif

➤!Médianes de survie après traitement palliatif seul : 1-2 mois

- anticonvulsivants
- corticoïdes
- mannitol
- valve ventriculo-péritonéale

J. Natl. Cancer Inst. 2011;103:820-836
Irradiation of Brain Tumors in Dogs with Neurologic Disease
Carla Eolner Bley, Andreu Simova, Malgorzata Roos, and Barbara Kuest-Horx



Traitement des tumeurs intra-crâniennes

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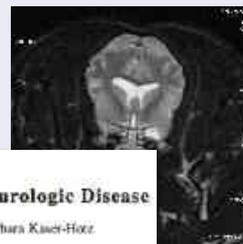
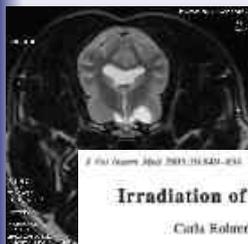
Radiothérapie
Gliomes

Tumeurs gliales canines

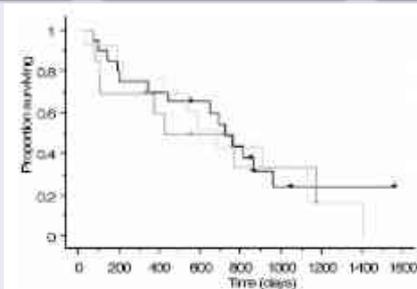
CN boxer F 8a!

+ 8 mois!

+ 14 mois!



J. Natl. Cancer Inst. 2011;103:820-836
Irradiation of Brain Tumors in Dogs with Neurologic Disease
Carla Eolner Bley, Andreu Simova, Malgorzata Roos, and Barbara Kuest-Horx



Méningiomes canins

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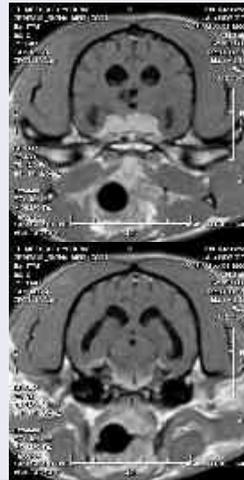
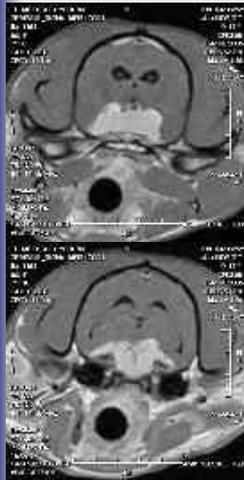
Gliomes

Méningiomes

CN croisé M 13a!

+ 5 mois!

+ 9 mois!



Méningiomes canins

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Gliomes

Méningiomes

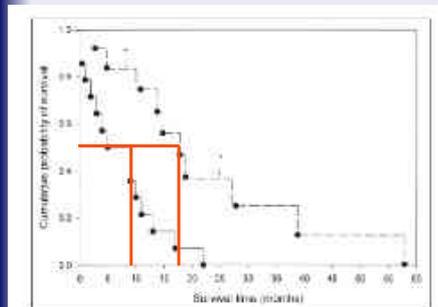
Surgery alone or in combination with radiation therapy for treatment of intracranial meningiomas in dogs: 31 cases (1989-2002)

JAVMA, Vol 221, No. 11, December 1, 2002

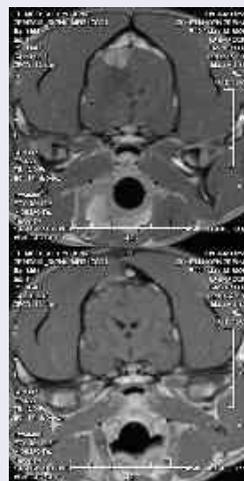
Tufts W. Aronoff, et al. / JAVMA, Vol 221, No. 11, December 1, 2002

CN labrador F 11a!

Médianes de survie : 7 vs 16,5 mois



+ 8 mois!



Méningiomes canins

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Epidémiologie
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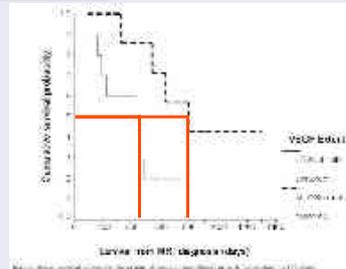
Influence of tumor cell proliferation and sex-hormone receptors on effectiveness of radiation therapy for dogs with incompletely resected meningiomas.
Theon AP, Lecouteur RA, Carr EA, Griffey SM.
J Am Vet Med Assoc 2000;216: 701-707

PF_{PCNA} faible vs élevée :
survie à 2 ans 93% vs 42%

Radiothérapie
Gliomes
Méningiomes

Vascular Endothelial Growth Factor Expression in Canine Intracranial Meningiomas and Association with Patient Survival
Simon R. Platt, Timothy J. Scarz, Vaski Adams, Lara Wisniewski, Judi Miller, Filippo Adorni, and Sam Long

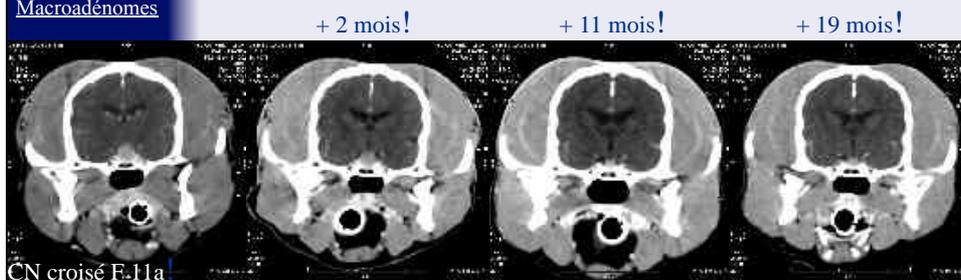
Expression VEGF faible vs élevée :
Médiane de survie 25 vs 15 mois



Macroadénomes canins

Introduction
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Méningiomes
Macroadénomes

Auteur	Nbre chiens	Source	Dose totale	Protocole	Médiane survie
Dow et coll.	7	6 MeV	40 Gy	10 x 4Gy	106 sem
Mauldin et coll.	10	Cobalt-60	54 Gy	18 x 3Gy	10 sem
Théon et coll.	24	Cobalt-60	48 Gy	12 x 4Gy	46 +/- 23 sem
Kent et coll.	19	4 MeV	48 Gy	16 x 3Gy	> 285 sem



Traitement des tumeurs intra-crâniennes

Effects of radiotherapy on pituitary corticotroph macrotumors in dogs: A retrospective study of 12 cases

Pauline de Fornel, Françoise Delisle, Patrick Devauchelle, Dan Rosenberg *Can Vet J* 2007;48:481-486

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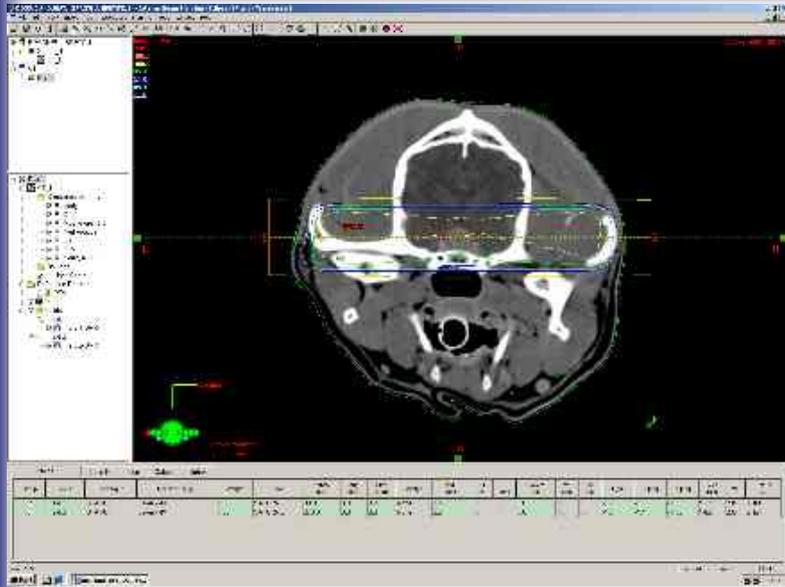
Diagnostic

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Traitement des tumeurs intra-crâniennes

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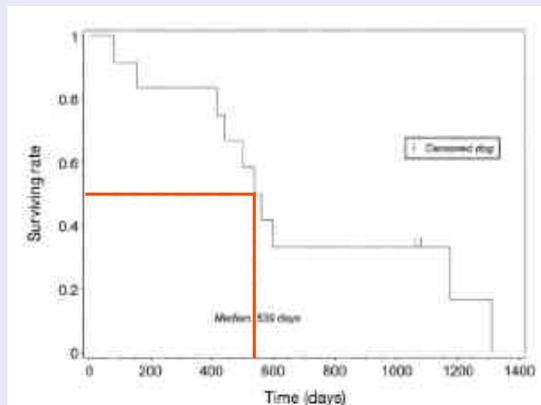
Diagnostic

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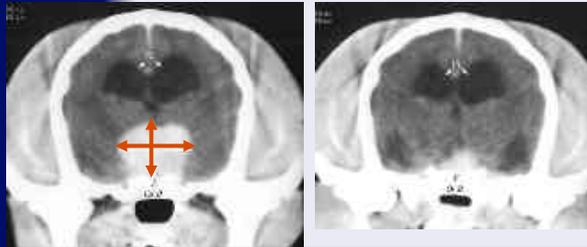
Macroadénomes



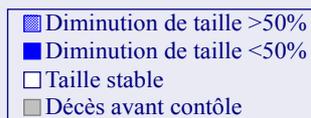
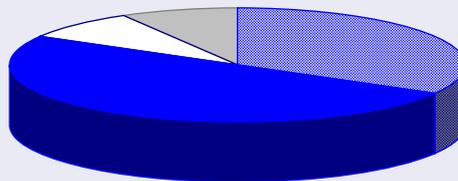
77 semaines

➔ **Suivi tomodensitométrique**

+ 2 mois



➔ **Suivi tomodensitométrique**



✓! Régression de la tumeur objectivée dans les 5 premiers mois.

✓! Régression durable jusqu'à 28 mois post-radiothérapie.

Effects of radiotherapy on pituitary corticotroph macrotumors in dogs: A retrospective study of 12 cases

Pauline de Fornel, Françoise Delisle, Patrick Devauchelle, Dan Rosenberg *Can Vet J* 2007;48:481-486

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➔ **Suivi tomodensitométrique**

- ✓! Récidive chez 4 chiens, entre 7 et 19 mois post-radiothérapie.
- ! Réirradiation

+ 2 mois

+ 7 mois



Effects of radiotherapy on pituitary corticotroph macrotumors in dogs: A retrospective study of 12 cases

Pauline de Fornel, Françoise Delisle, Patrick Devauchelle, Dan Rosenberg *Can Vet J* 2007;48:481-486

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+ 2 mois

+ 7 mois



Adénomes hypophysaires félines et acromégalie

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Epidémiologie

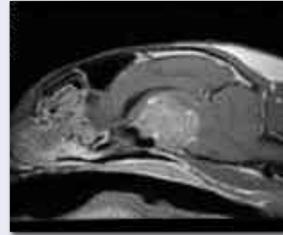
Diagnostic

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Macroadénomes



- ✓!Diminution des besoins en insuline chez 37 des 47 chats traités
- ✓!Arrêt de l'insulinothérapie chez près de 50 % des chats traités
- ✓!Suivi par imagerie de 5 chats uniquement...

Brearley et al. Vet Comp Oncol 4:209-217, 2006.
Goossens et al. J Am Vet Med Assoc 213:374-376, 1998.
Kaser-Hotz et al. J Small Anim Pract 43:303-307, 2002.
Littler et al. J Small Anim Pract 47:392-395, 2006.
Mayer et al. J Vet Intern Med 20:1151-1154, 2006.
Peterson ME et al. J Vet Intern Med 4:192-201, 1990.
Sellon et al. J Vet Intern Med 23:1038-1044, 2009.

Lymphomes cérébraux félines

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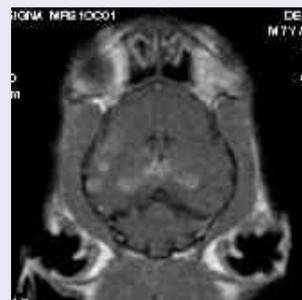
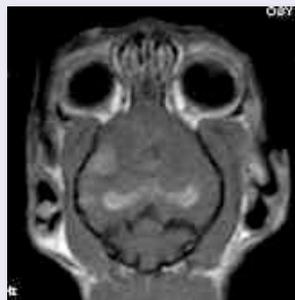
Radiothérapie

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Méningiomes

Macroadénomes

Lymphomes



1 semaine après L-asparaginase

- ✓!un lymphome cérébral primitif : 3 x 8 Gy, survie 210 jours.
- ✓!un lymphome général : 2 x 5 Gy + chimiothérapie, survie 40 jours.
- ✓!deux lymphomes généraux : chimiothérapie seule, survie 2-4 jours.

Noonan et al. Comp Contin Educ 19:497-503, 1997.

Traitement des tumeurs intra-crâniennes

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Gliomes
Méningiomes
Macroadénomes
Lymphomes

Chimiothérapie

✓!Cytosine arabinoside (polychimiothérapie).
✓!Lomustine.

- !2 tumeurs : lomustine seule, survie 2 et 16 mois
- !2 gliome : chirurgie puis lomustine, survie 2 et 21 mois
- !1 astrocytome : chirurgie puis lomustine, survie 3 mois
- !2 méningiomes : chirurgie puis lomustine, survie 1 et 7 mois
- !1 méningiome : lomustine et corticoïdes, survie 13 mois

✓!Hydroxyurée.

- !1 méningiome : hydroxyurée et corticoïdes, survie 14 mois, diminution de taille de la tumeur à 1 mois



Fulton and Steinberg. Seminars Vet Med Surg 5:241-245, 1990.
Jung et al. J Vet Med Sci 68:383-386, 2006.
Tamura et al. J Vet Med Sci 69:1313-1315, 2007.
Noonan et al. Comp Contin Educ 19:497-503, 1997.

Traitement des tumeurs intra-crâniennes

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Macroadénomes
Lymphomes

Chimiothérapie

Traitement palliatif

Conclusion

- !Une démarche diagnostique incomplète
- ! Une conduite thérapeutique hétérogène
- !Evolution des données corrélant imagerie et anatomopathologie
- !Démocratisation des outils diagnostiques et de suivi
- !Développement de nouveaux outils diagnostiques
- !Place de la radiothérapie dans le traitement des tumeurs intracrâniennes canines et félines
- !Pistes thérapeutiques...

Microarray Analysis of Differentially Expressed Genes of Primary Tumors in the Canine Central Nervous System

S. A. M. THOMPSON, F. KENNEDY, N. O'DAY, J. R. MICKELSON, D. E. HOLTMANN, P. J. DICKINSON, C. GIBSON, AND M. BIRER

Diagnostic génétique: vers une thérapie ciblée

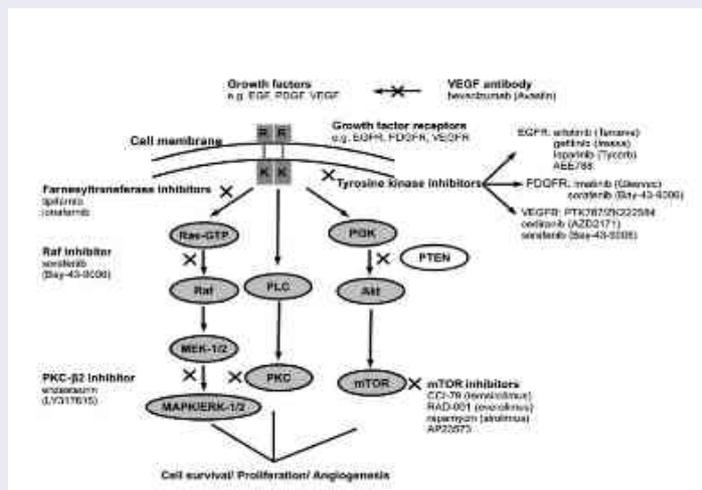
Table 3: List of differentially expressed genes with a fold change of three or greater in canine meningioma samples (see SOM Table 4 for a more complete list of the data).

Gene Name	Fold Change*	P-Value	Gene Acc No	Gene ID
PODX1	-3	8.96E-05	BQ091456	5420
NCAM	-3	4.07E-06	BQ091464	4684
CRFG	-3	3.09E-05	BQ091879	8804
TAMP1	+18	7.92E-06	BI395313	3916
RAB9	+15	1.09E-07	CFRAB9	403947
UBA52	+13	3.89E-05	CTA388512	7311
NT1	+13	4.84E-05	D84397	403800
RPUB1	+11	1.18E-08	BQ839561	281370
TCEB1L	+8	3.95E-05	BI395330	6500
RPL15	+8	4.90E-05	NML002948	6138
PRDX1	+7	1.85E-05	NML002574	5052
RPL9	+7	6.51E-06	BQ091592	6135
YWHAE	+6	3.58E-06	BQ091814	7521
RPL9	+6	3.42E-05	BQ091592	6133
RPL19	+5	5.47E-05	CTA388522	403682
NPEG1	+5	2.26E-05	BI395335	119972
EEF1A1	+5	1.00E-05	AY195837	403506
RPS25	+4	1.13E-05	BI817150	6230

Molecularly Targeted Therapies for Malignant Gliomas

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