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Radiation Therapy for Intracranial Tumors in Cats with Neurologic Signs

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Abstract

The objective of this retrospective multicenter study was to evaluate the outcome of 22 cats with intracranial tumors presenting with neurologic signs and/or epileptic seizures treated with radiation therapy.

In the treated cats we investigated patient-, tumor- and treatment-related variables for influence on local tumor control and survival. Based on advanced imaging characteristics, the treated cats presented with meningioma (n=11), pituitary tumor (n=8), choroid plexus tumor (n=2), or glioma (n=1). Allocated to the neuraxis, 11 lesions were extra-axial, 3 intra-axial and 8 were located in the pituitary region. At diagnosis, 21 cats exhibited altered neurological status. One cat presented with epileptic seizures and another cat had both seizures and altered neurological status. The mean total physical dose of radiation was 41.63 Gy (± 4.33), range 24-45 Gy. In all but one cat (95.5%), neurological signs improved after radiation therapy. The median progression free survival was 510 days (95% CI: 51-969). The median overall survival time was 515 days (95% CI: 66-964). None of the tested variables influenced outcome.

Radiation therapy seems to represent a viable treatment option in cats with intracranial tumors, relieving neurological signs and improving local tumor control. Radiation therapy may be considered for cats with tumors in complicated/inoperable localizations or for cases with a high peri- and postoperative risk.

Keywords: brain tumor, meningioma, glioma, radiation therapy, pituitary

Vetsuisse-Fakultät, Universität Zürich (2018)

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Radiation Therapy for Intracranial Tumors in Cats with Neurologic Signs

Zusammenfassung

In dieser retrospektiven multizentrischen Studie wurden die Folgen einer Strahlentherapie bei 22 Katzen mit einem intrakraniellen Tumor und mit neurologischen Symptomen und/oder epileptischen Anfällen evaluiert.

Es wurden die patienten-, tumor- und behandlungsrelevanten Variablen auf ihren Einfluss auf die lokale Tumorkontrolle und das Überleben untersucht. Beruhend auf der Befundung der Bildgebung wurden die Katzen mit Meningiomen (n=11), Hypophysen Tumoren (n=8), Choroid Plexus Tumoren (n=2) oder Gliomen (n=1) diagnostiziert. Bei der Diagnose zeigten 21 Katzen einen veränderten neurologischen Zustand. Eine Katze wurde mit epileptischen Anfällen und eine weitere mit epileptischen Anfällen und verändertem neurologischen Zustand vorgestellt. Der Mittelwert der Gesamtdosis war 41.63 Gy (± 4.33), mit einer Breite von 24-45 Gy. Ausser in einem Fall (95.5%) verbesserten sich die neurologischen Symptome nach der Therapie. Die mittlere progressionsfreie Überlebenszeit lag bei 510 Tagen (95% CI: 51-969). Die mittlere Überlebenszeit betrug 515 Tage (95% CI: 66-964). Keine der untersuchten Variablen beeinflusste das Ergebnis.

Strahlentherapie scheint eine nützliche Behandlung für Katzen mit intrakranialen Tumoren zu sein, führt zur Linderung der neurologischen Symptomatik und optimiert die Tumorkontrolle. Eine Bestrahlung sollte besonders in komplizierten, nicht operablen Bereichen, sowie bei Fällen mit einem erhöhten peri- und postoperativen Risiko in Betracht gezogen werden.

Schlüsselwörter: Hirntumor, Meningiom, Gliom, Strahlentherapie, hypophysär

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SAGE

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Abstract

Objectives The aim of this study was to evaluate the outcome of cats with intracranial tumours presenting with neurological signs treated with radiation therapy.

Methods This study comprised a retrospective multi-centre case series. Medical records of a total of 22 cats with intracranial space-occupying lesions, presenting with neurological signs and/or epileptic seizures and treated with external beam radiation therapy, were reviewed. In the treated cats, patient-, tumour- and treatment-related variables were investigated, including age, sex, tumour location, tumour volume, total radiation dose, equivalent dose in 2 Gy fractions (EQD_2), corticosteroid dose, overall treatment time and institution for influence on local tumour control and survival.

Results Based on advanced imaging characteristics, the 22 treated cats presented with meningioma (n = 11), pituitary tumour (n = 8), choroid plexus tumour (n = 2) or glioma (n = 1). Allocated to the neuraxis, 11 lesions were extra-axial, three intra-axial and eight were located in the pituitary region. At diagnosis, 21 cats exhibited altered neurological status. One cat presented with epileptic seizures and another cat had both seizures and altered neurological status. The mean total physical dose of radiation was 41.63 Gy (± 4.33), range 24–45 Gy. In all but one cat (95.5%), neurological signs improved after radiation therapy. The median progression-free survival was 510 days (95% confidence interval [CI]: 51–969). The proportion free of progression at 1 year was 55.7% (95% CI: 33–78). Fourteen cats died (only in five cases was death related to the intracranial tumour) and eight cats were still alive or lost to follow-up. The median overall survival time was 515 days (95% CI: 66–964). None of the tested variables influenced outcome.

Conclusion and relevance Radiation therapy seems to represent a viable treatment option in cats with intracranial tumours, relieving neurological signs and improving local tumour control. Radiation therapy may be considered for cats with tumours in complicated/inoperable localisations or for cases with a high peri- and postoperative risk.

Keywords: Brain tumour; meningioma; glioma; radiation therapy; intracranial; radiotherapy; pituitary

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Introduction

Neurological signs in cats with primary intracranial tumours are common and include altered consciousness (36.8%), circling (31.6%) and epileptic seizures (31.6%).[1] Symptomatic therapy such as corticosteroids and/or antiepileptic medications provides only short-term relief. Prognosis in these conservatively managed patients is poor, with reported survival of 18 days.[1–3] Complete or partial eradication of the tumour with surgery is desired in the management of intracranial disease and often results in improvement or resolution of neurological signs.

The most frequently occurring brain tumour in cats is meningioma.[1,4] Feline meningioma is often non-invasive (World Health Organization grade 1) and located peripherally in the calvarium,[1,4] which often makes surgery the treatment of choice. Surgical excision results in favourable long-term outcomes with a median survival of 22.8–37 months.[1,2,5] However, invasive tumours or tumours located at non-peripheral locations within the calvarium may be difficult to remove or may not be amenable to surgery.[3] Treatment options for cats with inoperable intracranial tumours are not well described. In dogs with primary intracranial neoplasia of any type presenting with neurological signs, radiation therapy is considered to be one of the treatments of choice. After radiation therapy, an improvement within 6 months or resolution of neurological signs associated with a long-term survival in the range of 2 years is observed in dogs with brain tumours.[6–9] In cats, response to ionising radiation and subsequent tumour control are not known. The few studies that describe response to radiation therapy in cats presented with neurological signs caused by an intracranial tumour are limited to pituitary tumours but indicate that neurological amelioration can occur.[10–13]

In this retrospective multicentre cases series, we describe the progression-free survival (PFS) and overall survival (OS) in cats with intracranial tumours presented with neurological signs after treatment with radiotherapy (RT). We investigated the influence of patient-, tumour- and treatment-related variables on local control and survival.

Materials and methods

Patients

The databases of the Division of Radiation Oncology of the Vetsuisse Faculty, University of Zurich (Switzerland), the Centro Oncologico Veterinario (Italy), the Royal (Dick) School of Veterinary Studies, Radiation Oncology Department, University of Edinburgh (UK) and the University of Wisconsin-Madison Veterinary Medical Teaching Hospital (USA) were searched for cats with primary, non-lymphoid intracranial space-occupying lesions with imaging diagnosis of a tumour, presented with neurological signs that had been treated with radiation therapy alone between January 2002 and June 2017. Cats that had undergone surgery (complete excision or debulking) or received any type of systemic anticancer treatment such as chemotherapy were excluded from the study. Contributing veterinary radiation oncologists were asked to collect information from the medical record of each case including signalment, neurologic signs, diagnostic tests, tumour localisation, and imaging-based diagnosis, medical management (ie, corticosteroids), radiation therapy protocol and survival time.

The space-occupying lesions in the brain were diagnosed by a board-certified radiologist either by contrast-enhanced CT or MRI. Due to the lack of histological diagnosis, the lesions were allocated to one of three groups according to their imaging characteristics: a) extra-axial tumours (consistent with meningioma, schwannoma and choroid plexus tumour), b) intra-axial tumours (consistent with glioma) and c) pituitary tumours (consistent with adenoma and adenocarcinoma of the pituitary gland).[7,14] A second grouping was made according to the location of the tumour relative to calvarial anatomy: a) rostral cranial fossa (rostral to the optic chiasm), b) middle cranial fossa (between the optic chiasm and the dorsum sellae and petrosal crests, pituitary/temporal region) and c) caudal cranial fossa (between the dorsum sellae and petrosal crests and the foramen magnum, including brainstem and cerebellum).[15] Lesions suspicious for lymphoma (based on diagnostic imaging criteria) were excluded.[14]

The patient's neurological signs at the time of diagnosis were grouped into three categories: a) patients with altered neurologic status (changes in mentation and behaviour, gait and postural abnormalities, deficits of cranial nerves including central blindness and head tilt), b) patients with only epileptic seizures and c) patients with epileptic seizures and altered neurologic status. Other information recorded included medical treatment at the time of diagnosis, findings regarding tumour staging and, if available, cerebrospinal fluid analysis.

Treatment

All cats were treated with external beam megavoltage radiation therapy. Radiation was delivered with 6 MV linear accelerators (Dynaray LA20 [ABB/Varian], Clinac DMX or Clinac iX [Varian Medical Systems], Clinac 2100 C/D [Varian Medical Systems]).

Treatment planning was performed by a board-certified veterinary radiation oncologist in all cases, on the basis of three-dimensional (3D)-CT datasets and using computerised radiation treatment planning systems (Cadplan [precursor versions of Eclipse], Eclipse External Beam Planning system version 8.6, 10.0 and 11.0; Varian Oncology Systems). Treatment planning CT scans were performed with each patient in the treatment position using a customised immobilisation device according

to each institution's standard practice.[16] The gross tumour volume (GTV) was defined as the abnormal contrast-enhancing tissue on CT or MRI images. The clinical tumour volume (CTV) was added at the radiation oncologist's discretion and a planning target volume (PTV) was added to include a safety margin accounting for systematic and random uncertainties. Organs at risk (normal brain tissue and eyes) were contoured in all cats.

Radiation treatment was planned isocentrically using photons and 3D conformal radiation therapy. Beam shaping devices such as lead blocks, multi-leaf collimators and wedges were used to improve homogeneity and to minimise dose to organs at risk. In general, the dose was prescribed according to the International Commission on Radiation Units & Measurements.[17,18] Irradiation was delivered in various fractionated regimes.

Follow-up

Contributing veterinary radiation oncologists gathered the post-RT follow-up information from the patients' records. If a follow-up diagnostic imaging study was available, tumour response was quantified according to the response evaluation criteria in solid tumours (RECIST) guidelines for dogs.[19] The sum of diameters of all target lesions was calculated and reported as the baseline sum diameter. Complete remission (CR) was defined as the disappearance of all target lesions. Partial response (PR) was defined as a reduction of at least 30% in the sum of diameters of target lesions from baseline. Progressive disease (PD) was defined as an increase in the sum of diameters of target lesions by at least 20% over baseline, or the appearance of new lesions. Tumours that showed neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD were considered to be of stable disease (SD). For cats that were not re-evaluated at one of the participating centres, the referring veterinarians and owners were queried by telephone regarding performance status, neurological signs compared with those at the time of diagnosis, disease progression and date of death by one of the authors (MKO, MPA or SCA).

Statistical analysis

Statistical evaluation was performed under the supervision of a biostatistician (MR) and computed with a commercial statistical software package (IBM SPSS Statistics, Version 24). Data were used as submitted in an Excel table by the contributing veterinary radiation oncologists. Description of quantitative data characteristics, other than PFS and overall survival OS, is given by mean (± SD), unless otherwise specified. Description of qualitative characteristics is provided in absolute and relative frequencies.

PFS was defined as the interval between the first day of radiation therapy to measurable progression of disease, worsening of neurological signs compared with the neurological status before RT, or death. OS was defined as the interval between the first fraction of radiation therapy and death. Cats that were free of progression of measurable tumour and of progression of neurological signs and that were alive at the time of data collection were censored for PFS analysis. For OS, all deaths were considered events and cats that were still alive at the time of data collection or lost to follow-up were censored at the last date of contact.

Kaplan-Meier survival analysis was used and followed by Logrank test. The univariate Cox-regression analysis was used to determine whether the following factors were associated with PFS or OS: age, sex, meningioma/non-meningioma, meningioma/ pituitary tumour, tumour volume (GTV, GTV/brain ratio), treatment volume (PTV, PTV/brain ratio), tumour location, treatment institution, dose of radiation (total dose, equivalent dose in 2 gray (Gy) fractions [EQD_2]), dose of corticosteroids at first RT fraction, overall treatment time (counted from the first to the last fraction of RT). The EQD_2 was used to compare the different radiation protocols. Survival estimates at a certain time point are presented as a percentage with the corresponding 95% confidence intervals (95% CI). Median survival time estimates are complemented with 95% CI. The paired Wilcoxon test evaluated the change in corticosteroid dose from the first to the last RT fraction. Results of statistical analyses with P value <0.05 were interpreted as statistically significant.

Results

Patient and tumour characteristics

Twenty-two cats met the inclusion criteria for this study. Nine of the cats were female (nine were spayed) and 13 were male (12 were castrated). The presented breeds included domestic shorthair (n = 18), Persian (n = 3) and Selkirk Rex (n = 1). The mean age was 12.0 years (± 2.3) and ranged from 6.5–16.4 years. The mean body weight was 4.5 kg (± 1.4) and ranged from 2.3–8.3 kg. Fifteen animals were treated at the Division of Radiation Oncology of the Vetsuisse Faculty, University of Zurich, Switzerland, six animals at the Centro Oncologico Veterinario, Sasso Marconi, Bologna, Italy, and one animal was treated at the Royal (Dick) School of Veterinary Studies Radiation Oncology Service, University of Edinburgh, UK. There were no cats that met the inclusion criteria from the University of Wisconsin-Madison Veterinary Medical Teaching Hospital, USA.

Based on imaging characteristics, tumours were diagnosed as meningioma (n = 11), pituitary tumour (n = 8), choroid plexus tumour (n = 2) or glioma (n = 1). Eleven tumours were considered extra-axial, three intra-axial and eight were located in the pituitary region. Tumours were distributed in the cranial fossa

Table 1 Individual patient data regarding tumour type and size, radiation protocols, progression-free survival (PFS) and overall survival (OS)

Case	Age (years)	Sex	Tumour type‡	GTV (cm^3)	Number of fractions	Treatment schedule	Dose/ fraction (Gy)	Total dose (Gy)	EQD_2 (Gy_2)	PFS (days)	OS (days)
1	8	mc	Meningioma	4.19	10	Daily	4	40	46.7	204*	204*
2	13	mc	Meningioma	0.51	10	Daily	4	40	46.7	121*	121*
3	11	fs	Meningioma	0.86	14	Daily	3	42	45.5	740	963†
4	11	fs	Meningioma	1.60	18	Daily	2.5	45	46.9	50	50
5	14	fs	Meningioma	0.15	14	Daily	3	42	45.5	63	63
6	12	mc	Meningioma	0.61	19	Daily	2.25	42.75	43.6	225*	225*
7	10	mc	Meningioma	3.49	20	Daily	2.25	45	45.9	535	540¶
8	10	mc	Meningioma	2.35	20	Daily	2.25	45	45.9	515	520¶
9	11	fs	Meningioma	7.70	20	Daily	2.25	45	45.9	510	515¶
10	14	fs	Meningioma	1.10	14	Daily	2.9	40.6	43.6	91	91
11	14	mc	Meningioma	2.35	20	Daily	2.25	45	45.9	174	174
12	13	mc	Pituitary gland tumour	2.55	10	Daily	4	40	46.7	839*	839*
13	16	mc	Pituitary gland tumour	0.72	10	Daily	4.2	42	49.7	55	55
14	13	mc	Pituitary gland tumour	1.17	14	Daily	3	42	45.5	70	70
15	12	fs	Pituitary gland tumour	0.82	10	Daily	4.2	42	49.7	644*	644*
16	7	m	Pituitary gland tumour	1.42	17	Daily	2.5	42.5	44.3	76*	76*
17	12	mc	Pituitary gland tumour	1.20	14	Daily	3	42	45.5	775	1056†
18	12	mc	Pituitary gland tumour	2.10	14	Daily	3	42	45.5	144	144¶
19	11	fs	Pituitary gland tumour	1.44	20	Daily	2.25	45	45.9	99	99
20	12	mc	Choroid plexus tumour	0.17	3	MWF	8	24	36.0	558*	558*
21	15	fs	Choroid plexus tumour	1.60	10	Daily	4	40	46.7	265	276¶
22	14	fs	Glioma	1.01	10	Daily	4.2	42	49.7	575*	575*

m = male; mc = male castrated; fs = female spayed; GTV = gross tumour volume; EQD_2 = equivalent dose delivered in 2 Gy fractions; MWF = Monday-Wednesday-Friday

*Cats free of progression and alive at the time of data evaluation or lost to follow-up were censored

†Cats were re-irradiated at the time of progression and censored from analysis of OS at the start of the second course of radiation therapy

‡Tumour type is based on advanced imaging characteristics

¶Died of tumour-or treatment-related causes

(n = 9), middle fossa (n = 8) or caudal fossa (n = 5). The pretreatment tumour volumes (GTV, absolute tumour size) had a mean of 1.78 cm^3 (± 1.67) with a range of 0.15–7.70 cm^3. Mean GTV/brain ratio (relative tumour size, [n = 16]) was 8.32 % (± 8.55) and the PTV/brain ratio could be derived for 16 cats with a mean of 33.18 % (± 34.00). The majority of cats presented with altered neurological status and without epileptic seizures (n = 20). One cat presented with epileptic seizures only (Table 1, case 22) and one cat with both altered neurological status and epileptic seizures (Table 1, case 21).

Treatment

Twenty-one patients were treated with various definitive-intent daily-fractionated protocols (Table 1). One patient (Table 1, case 20) was treated with a highly conformal definitive-intent hypofractionated radiation protocol (3 X 8 Gy) delivered every other day and received less than 40.00 Gy of total dose. Total doses ranged from 24.00–45.00 Gy, with a mean total dose of 41.63 Gy (± 4.33). Fraction sizes ranged from 2.25–8.00 Gy, with a mean of 3.32 Gy (± 1.29). Twenty-one cats were treated using a daily (Monday-Friday) treatment schedule. Only case 20 (Table 1) was treated on a Monday-Wednesday-Friday schedule. All

cats completed the full course of the planned radiation therapy. The respective EQD_2 were 36.00–49.70 Gy_2, with a mean of 45.79 Gy_2 (± 2.74). Mean overall treatment time was 19.6 days (5–29 days).

Pretreatment corticosteroid treatment with prednisolone was given to 20/22 cats with a mean dose of 0.66 mg/kg (± 0.41) q24h PO and tapered to mean doses of 0.58 mg/kg (± 0.43) q24h PO post-RT ($P = 0.076$). Three cats received antiepileptic treatment consisting of either phenobarbital (n = 2) or levetiracetam (n = 1) pre-, during and post-RT. Two of these cats had epileptic seizures at initial presentation and one received phenobarbital prophylactically and was tapered off the medication after RT, as no epileptic seizures were observed.

Outcome and prognostic factors

Median follow-up time for censored cases (n = 8, still alive or lost to follow-up) was 575 days (95% CI: 464–686). Fourteen of the 22 cats died during the study period. Death was attributed to the brain tumour or possible treatment-related toxicity in 5/14 cats (35.7%). In the 64.3% of animals that died due to other causes, death was related to other neoplastic disease (n = 4, histiocytic sarcoma in the liver [Table 1, case 4], lymphosarcoma in the bladder [Table 1, case 5], oral sarcoma [Table 1, case 10], intestinal lymphoma [Table 1, case 13]), and tumour-unrelated medical problems (not accompanied with neurological symptoms) such as hyperthyroidism (Table 1, case 11), cardiac failure with dilated atria, arrhythmia and mild pericardial effusion (Table 1, case 14) or pyothorax (Table 1, case 19). In two cases (Table 1, cases 3 and 17) the cats died at home with general weakness. Tumour recurrence could not be ruled out because no necropsy was performed, so the real cause for death remains unknown in these two cases.

Based on medical records and owner communication, clinical and neurological status improved in 21/22 (95.5%) cats, compared with the pre-treatment complaints. One of the 22 cats was judged to have stable clinical signs (Table 1, case 18). In the patient in which epileptic seizures was the only presenting complaint, it was difficult to determine whether seizure control was attributable to reduction of tumour/oedema or to anti-epileptic medication.

A total of 10 post-RT diagnostic imaging examinations were performed in six patients. CT was performed four times (n = 3 cats), and MRI was performed six times (n = 3 cats). On MRI, one cat with a meningioma showed partial remission at 6 months post-RT (Table 1, case 1), a second cat with a meningioma showed stable disease at 3, 6 and 12 months post-RT (Table 1, case 6). Another cat with a pituitary gland tumour showed stable disease on MRI at 6 and 12 months post-RT (Table 1, case 12). In the CT of one cat 6 months post-RT, the tumour was in partial remission (the 12 month re-check CT of the same cat was made at another clinic and tumour volume was not measured) (Table 1, case 15). Tumours of two cats were measured 24 months post-RT; one cat still showed stable disease (Table 1, case 17) and the other cat was scanned upon re-occurrence of neurological signs and was found to have a disease progression on CT (Table 1, case 3). Overall, seven cats (31.8%) were considered to have a disease progression either of increased volume based on imaging (n = 1) or of progression of neurological signs (n = 6).

The median PFS time for all 22 cases was 510 days (95% CI: 51–969). The proportion free of progression at 1 year was 55.7% (95% CI: 33–78) (Figure 1). Of the nine cats that died within the first year after RT, seven (77.8%) died of causes unrelated to the brain tumour (Table 1, cases 4, 5, 10, 11, 13, 14 and 19) and two (22.2%) died because of the brain tumour or treatment-related toxicity (Table 1, cases 18 and 21). No difference was seen in PFS between the patients treated at the different institutions ($P = 0.634$). At the time of tumour progression, two cats were re-irradiated, resulting in an additional progression-free interval of 223 and 281 days (Table 1, cases 3 and 17). Both cases were censored from analysis of OS at the start of the second course of radiation therapy. Neither the patient-related (age, sex), tumour-related (meningioma/non-meningioma, meningioma/pituitary tumour, tumour size, tumour location) nor treatment-related parameters (dose of radiation [total radiation dose or EQD_2], corticosteroid dose at first RT, overall treatment time, treatment institution) were associated with PFS.

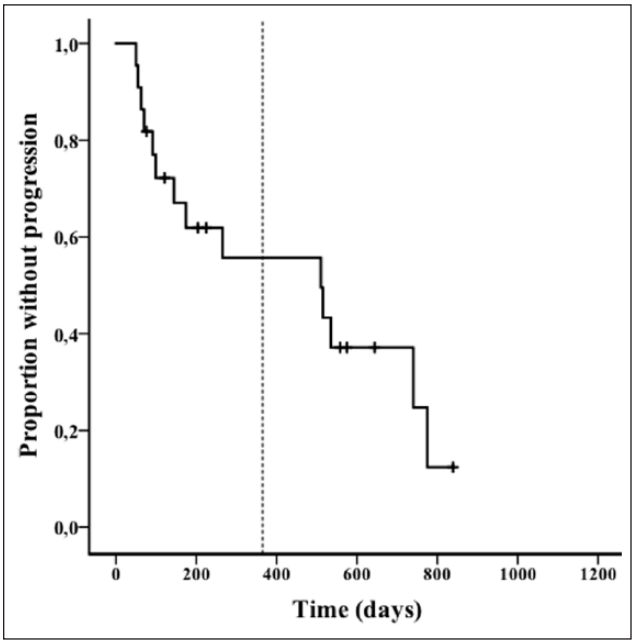

Figure 1 Median progression-free survival (PFS). The dotted line marks 1 year. Tick marks: cats that were free of progression of measurable tumour and of progression of neurological signs and that were alive at the time of data collection were censored for PFS analysis. Of the nine cats that died within the first year after radiotherapy, seven (77.8%) died of causes unrelated to the brain tumour and two (22.2%) died because of the brain tumour or treatment-related toxicity

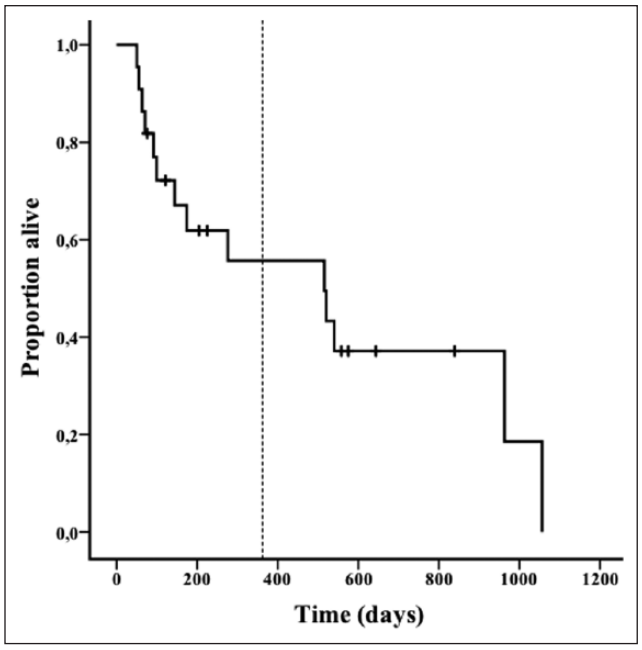

Figure 2 Median overall survival (OS): the dotted line marks 1 year. Tick marks: cats that were still alive at the time of data collection or lost to follow-up were censored at the last date of contact

Median OS was 515 days (95% CI: 66–964). The proportion alive at 1 year was 56 % (95% CI: 33–79) and at 2 years 37% (95% CI: 15–60) (Figure 2). No difference was seen in OS between the patients treated at the different institutions ($P = 0.695$). None of the tested variables had a statistically detectable influence on OS.

Discussion

Intracranial tumours causing neurological signs in cats are often of extra-axial and non-infiltrative nature and can be successfully treated with surgery.[1–5] Meningiomas with and without neurological signs are the most common intracranial tumours in cats and postoperative median survival times were found to range between 22.8 to 37 months.[1,2,5] For feline patients with tumours in less accessible locations, such as tentorially located meningiomas, survival time was found to decrease to 19 months postoperatively.[3] The risk of fatal intra- or postoperative complications ranged between 6–19%[2,3,5] and, depending on primary tumour location, the postoperative recurrence rate was 12–21%[1,2,5] and 100% for tentorial meningiomas[3]. In these retrospective studies, a selection bias of only including surgically amenable tumours should be considered.

For cats with inoperable tumours, however, literature findings are scarce and limited to cases of pituitary neoplasia and a case report of a cat with oligodendroglioma treated with radiation therapy.[10–13,20] Surprisingly, amelioration of neurologic symptoms was rapid and often complete in most cats and survival times increased from a median of 1.1–1.7 months if treated with corticosteroids only[1] to a range of 5.5–20.5 months after radiation.[10–13] These results are difficult to compare to our findings, as in the cats treated for pituitary tumours only, 38.9% had neurologic symptoms and most of them were treated because of pituitary-dependent endocrine disease. However, as is known from dogs with pituitary tumours treated with radiation therapy, radiation therapy also prolonged survival in non-neurologic patients by delaying the onset of neurologic signs.[21] In dogs with an intracranial primary tumour and neurologic signs, fractionated radiation therapy is often considered the treatment of choice with durable tumour control in the range of 19.2–25.2 months.[6–9]

In this study, the outcomes of cats with intracranial tumours presented with neurological signs were retrospectively compiled. Cases were sought from four institutions, and only three institutions could contribute patients. This fact indicates the scarcity of brain tumours in cats. After radiation therapy, the neurological status improved in all but one cat (95.5%). Median OS was 17.2 months, with 56% of cats alive at 1 year after therapy. Surprisingly, only seven patients (32%) were considered to have disease progression during the time of follow-up. Most patients (9/14) died of other neoplastic diseases or unrelated medical problems. Upon recurrence of disease, two cats in this cohort were re-irradiated and attained an additional progression-free interval of 7.4 and 9.2 months (Table 1, cases 3 and 17, respectively). None of the investigated factors such as age, sex, treatment institution, tumour location (extra-axial, intra-axial, pituitary), tumour type, tumour size, regions of brain affected, total dose, EQD_2, corticosteroid dose at first RT or overall treatment time were found to correlate with PFS or OS.

We acknowledge the following limitations of this study that should direct future research approaches. a) The cats were treated at different institutions, with various non-standardised radiation protocols in terms of fraction size, total dose, overall treatment times, target volumes and treatment planning practices, equipment and patient position verification. In order to not skew the data into a direction, we decided to keep patients treated with all fraction schedules in the investigated group. b) Standardised neurological evaluation, severity of neurological signs and routine follow-up diagnostic imaging were not available, which should constitute an important focus for further evaluation of tumour response to radiation therapy. c) Improvement of the clinical signs could – at least in part – also be attributed to medical supportive treatment such as corticosteroids. d) The patient population consisted of a heterogeneous group, with varying unconfirmed tumour types. Presumptive tumour diagnoses were made according to advanced diagnostic imaging techniques.[14] Most of the

tumours were meningiomas (50%) or pituitary adenomas (36%), which are commonly non-infiltrative and hence less aggressive. Furthermore, due to the limited number of patients, statistical analysis for each tumour type was not performed. e) The patients were referred for radiation therapy and the possibility of resectability was not uniformly judged. f) Due to the retrospective nature of the study and the lack of follow-up imaging it was not in every case possible to differentiate tumour progression from radiation toxicity as the cause of recurring neurological signs.

Conclusion

Findings of this study suggest radiation therapy as a viable treatment option for cats with intracranial tumours presented with neurological signs. Case selection should focus on inoperable disease or patients with an estimated high peri- and postoperative risk.

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