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Megavoltage irradiation of pituitary macrotumors in dogs with neurologic signs

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Objective—To assess the efficacy and determine prognostic factors of megavoltage irradiation for pituitary macrotumors in dogs with neurologic signs.

Design—Prospective clinical trial.

Animals—24 dogs with pituitary macrotumor syndrome; 19 ACTH-secreting and 5 clinically endocrine-inactive tumors.

Procedure—Dogs were treated with 48 Gy of radiation during 4 weeks on an alternate-day schedule of 4 Gy/fraction. Three (12.5%) dogs did not complete the planned treatment because of progression of neurologic signs.

Results—A significant correlation was found between relative tumor size (ie, size of tumor relative to calvarium size) and severity of neurologic signs and between relative tumor size and remission of neurologic signs after irradiation. In dogs with pituitary-dependent hyperadrenocorticism, a significant correlation was found between relative tumor size and plasma endogenous ACTH concentrations. Prognostic factors that independently affected duration of remission of neurologic signs were relative tumor size and endocrine activity. The prognostic factor of duration of eucortisolemia was not found. Use of a large field of irradiation was associated with substantial damage to brain tissue.

Clinical Implications—Because radiation therapy was effective for treatment of tumors of small relative size in dogs, early treatment of pituitary tumors should improve prognosis. Further improvements may be obtained using protocols in which higher total radiation doses and smaller radiation dose fractions are given. Irradiation was effective for long-term control of functional pituitary macrotumors and resulted in acceptably low complication rates when small fields of radiation were used. (J Am Vet Med Assoc 1998;213:225–231)

Macrotumors (ie, ≥ 1 cm diameter) of the pituitary gland are found uncommonly in dogs. These tumors may be functional (ie, producing ACTH) or clinically endocrine inactive.1,2 It has been estimated that almost all dogs with pituitary-dependent hyperadrenocorticism (PDH) have functional pituitary tumors. Approximately 30% of dogs with PDH have pituitary macrotumors, and 50% of these dogs develop neurologic abnormalities secondary to the space-occupying mass.1 Approximately 10% of pituitary macrotumors do not synthesize hormones that result in clinical signs.2 Regardless of any clinically detectable endocrine abnormalities, pituitary macrotumors may cause neurologic abnormalities that include focal signs (eg, visual defects, cranial nerve paralysis, head tilt) and generalized signs attributable to increased intracranial pressure (eg, abnormal behavior, altered mentation, seizures).

In people, current recommendations for treatment of macrotumors include radiation therapy used alone or after surgery to control neurologic signs caused by mass effect and to control hormone secretion. Primary irradiation is indicated for treatment of inoperable or advanced tumors causing bone destruction or cranial nerve paralysis, because complete resection is usually not possible and because attempts at radical removal are associated with high morbidity and mortality.

Anatomy of the pituitary gland in dogs and suprasellar extension of macrotumors preclude safe complete surgical excision.3 Radiation therapy is, therefore, the only potentially effective treatment for macrotumors. Efficacy of radiation therapy for functional pituitary tumors has been described in dogs.4,5 Treatment of clinically endocrine-inactive pituitary tumors has not been reported. In people, the role of radiotherapy is influenced by tumor size, suprasellar extension, surgical resectability, and tumor histology.6 Prognostic factors have not been described in dogs with pituitary tumors. Tumor size was not found to have prognostic value and, despite the large disparity in size of dogs treated, attempts have not been made to analyze effects of tumor size in relation to calvarium size. The purposes of the study reported here were to assess the efficacy of megavoltage irradiation for treatment of pituitary macrotumors in dogs with neurologic signs and to determine prognostic factors influencing response to treatment.

Material and Methods

Animals—Twenty-four dogs were considered eligible for enrollment in the study on the basis of neurologic signs caused by a pituitary macrotumor. A macrotumor was defined as a tumor in which the largest diameter was ≥ 1 cm. Each dog was evaluated by physical, neurologic, and radiologic examinations and endocrine assay. Dogs ranged from 6 to 15 years old (mean, 9 years) and from 2 to 44 kg (4.4 to 97.0 lb; mean, 18 kg [39.7 lb]). Fifteen dogs were female, and 9 were male. Sixteen dogs were purebred; the most represented breeds included Poodle (n = 3), Boxer (3), and Boston Terrier (3). Nine dogs were of mixed breeding.

Macrotumors extending dorsally from the sella turcica were diagnosed, using imaging techniques that included contrast-enhanced computed tomography (CT; n = 16) or magnetic resonance imaging (MRI; 8). Tumor volumes were estimated, using the following equation:

\[ V = \pi \times \text{width} \times \text{length} \times \text{height}/6 \]

where \( \pi = 3.14 \), and width, length, and height were the largest diameters obtained from CT or MRI images. Estimates of tumor volume ranged from 0.7 to 4.2 cm³ (mean, 1.9 cm³)
median, 2.1 cm). Relative tumor size (RTS) was calculated as the ratio of tumor area to cranial vault area measured from CT or MRI images that depicted the greatest tumor area. Estimates of RTS ranged from 4 to 26% (mean, 13%; median, 12%).

Tumor type was determined in 9 dogs on postmortem examination of histologic sections stained with H&E. Tumor types included 7 functional macroadenomas (4 chromophobe, 2 acidophil, and 1 basophil of the pars distalis) and 2 nonfunctional macroadenomas (1 chromophobe of the pars distalis and 1 of the pars intermedia). Four of 9 macroadenomas were invasive, extending up the pituitary stalk into the hypothalamus. Tumor growth resulted in compression of the hypothalamus in 3 dogs and of the optic chiasma in 2 dogs.

Nineteen dogs with ACTH-secreting pituitary tumors and 5 dogs with clinically endocrine-inactive pituitary tumors had neurologic signs attributable to mass effect. Four dogs with PDH also had central diabetes insipidus (CDI). Four of 5 dogs with clinically endocrine-inactive tumors had CDI.

Diagnosis of hyperadrenocorticism was established by documenting appropriate history and results of physical examination, CBC, serum biochemical analysis, psychiatric history, and abnormal results on at least 1 of the following 2 screening tests. ACTH stimulation test (ie, post-ACTH plasma cortisol concentration > 17 μg/dl, reference range, 5 to 17 μg/dl) and low-dose dexamethasone suppression test (8-hour postdexamethasone plasma cortisol concentration ≥ 1.4 μg/dl, reference range, < 1.4 μg/dl). Diagnosis of PDH was made on the basis of plasma cortisol concentration of endogenous ACTH ≥ 50 pg/ml (reference range, 20 to 100 pg/ml).

Pituitary-dependent hyperadrenocorticism was diagnosed 1 to 28 months before onset of neurologic signs (mean, 13 months; median, 11.5 months) and 3 to 31 months (mean, 14 months; median, 12 months) before radiation therapy. Fifteen dogs were treated with mitotane, as previously described, before radiation therapy. Of these dogs, 3 dogs were not in remission (based on results of an ACTH response test). In dogs with a response to exogenous ACTH that was within or below the reference range, plasma endogenous ACTH concentrations were 50 to 100 pg/ml in 2 dogs, 110 to 500 pg/ml in 5 dogs, and > 500 pg/ml in 5 dogs. Mitotane treatment was discontinued in all dogs before radiation therapy. In 9 dogs treated with mitotane, prednisone was given before irradiation to rule out mitotane toxicity (n = 1) or to improve neurologic signs (8).

Clinical neurologic signs included altered state of consciousness (signs of depression, n = 7; stupor, 5), abnormal behavior (pacing or disorientation, 7; circling, 5; anorexia, 4; incontinence, 3; head pressing, 3; aggression, 2), abnormal gait (mild ataxia, 4; mild paraparesis, 3; severe paraparesis, 1), and seizure (2). Focal neurologic signs included blindness (n = 2), anisocoria (3), facial paralysis (1), facial twitch (1), and head deviation (1). Central blindness was observed in 1 dog with, and another without, hyperadrenocorticism. Blindness was confirmed by documenting typical funduscopic examination findings and intraocular pressures by abnormal results on an electroretinogram. Other signs included body temperature dysregulation (shivering, n = 2; panting, 2). For purposes of analysis, neurologic status before irradiation was categorized as grade 1 (ie, seizures only or mild neurologic signs that were detectable by the owner or on neurologic examination) in 9 dogs, grade 2 (ie, moderate or marked neurologic signs, ambulatory) in 6 dogs, and grade 3 (stupor or nonambulatory) in 9 dogs.

Irradiation procedure—Each dog was anesthetized, and irradiation was performed with a telecobalt-60 unit, using an 80-cm source-skin distance. Computerized treatment planning was done on the basis of CT or MRI findings.

Irradiation was performed, using equally weighted parallel opposed fields. Treatment volume consisted of individualized portals designed to include the tumor and a 1.0- to 1.9-cm margin. Planned radiation dose was 40 Gy (minimum tumor dose) given in 12 fractions of 4 Gy/fraction during 4 weeks on an alternate-day schedule (ie, Monday, Wednesday, Friday). The dose was specified to the isodose line that encompassed the target volume, typically the 95% isodose line. Radiation portal sizes ranged from 9 to 36 cm (median, 25 cm). Twelve dogs received glucocorticoids during the course of irradiation. Eight dogs were treated with prednisone before and during the course of irradiation. Treatment with prednisone was instituted in 4 dogs during treatment because of deterioration of neurologic function. Two dogs with seizures were treated with phenobarbital and 6 dogs with CDI were treated with desmopressin acetate during radiation therapy.

Data analysis—Progression-free survival (PFS), overall survival, and acute and chronic radiation toxicoses were evaluated. Progression-free survival was defined as the time between the first day of irradiation and detection of progression of neurologic signs or death by causes unrelated to tumor progression, whichever came first. Overall survival was defined as the time between the first day of irradiation and death attributable to disease progression. Follow-up evaluations included serial serum biochemical analysis, ACTH stimulation testing, assay of plasma concentration of endogenous ACTH, MRI or CT imaging, and performance status. Clinical course consisted of the treatment period and a stable period defined as the time from the end of irradiation to disease progression. Tumor progression was evidenced by subjective determination of progression or recurrence of neurologic signs or increased tumor size on MRI (n = 4) or CT (2) examinations or at necropsy (10). Dogs that were alive without evidence of tumor progression or those that were dead of unrelated causes were censored at their last follow-up examination for calculation of PFS. In dogs with PDH, pituitary endocrine activity was considered controlled on the basis of clinical response and appropriate plasma concentration of cortisol after exogenous ACTH stimulation.

Variables examined as indicators of prognosis included age, sex, tumor subtype (ACTH secreting vs nonsecreting), plasma concentrations of endogenous ACTH from dogs with ACTH-secreting tumors, tumor volume, RTS, and severity of neurologic signs. Differences were analyzed, using Pearson’s χ² statistic for categorical variables, and ANOVA and correlation analysis for continuous variables. Survival and PFS distributions were computed, using the product-limit method. For multivariate analysis of PFS, the Cox’s proportional hazards regression model was used to determine significant prognostic factors. Relative risk of tumor progression was estimated by the hazard rate ratio. Comparisons were performed with a statistical software program. Differences were considered significant if P < 0.05.

Acute and chronic radiation toxicoses for superficial soft tissues were evaluated in all dogs. Brains from 9 dogs with recurring tumors and from 1 dog without signs of tumor recurrence were examined after death.

Results

Tumor characteristics—Tumor volume was significantly correlated with body weight; tumors with larger volumes were observed in larger-sized dogs (Fig 1). Tumor volume and RTS were independent of ACTH secretion, age, or sex. In dogs with PDH, a significant (r = 0.825; P < 0.0001) correlation was found between plasma concentration of endogenous ACTH and tumor volume (Fig 2). No correlation was observed between tumor volume and duration of tumor concentration.

Neurologic signs on clinical examination, neuromuscular function, and performance status of these 5 dogs with CDI were all improved, and 3 died during the first 24 months after completion of irradiation.
endogenous ACTH and RTS but not between plasma concentration of endogenous ACTH and tumor volume (Fig 2). Correlations were not found between duration of PDH and tumor size, RTS or plasma concentration of endogenous ACTH.

Neurologic signs—During the course of irradiation, neurologic signs deteriorated in 9 dogs. Four of these 9 had progressive disease without a stable period; 3 died during and 1 died shortly (23 days) after completion of radiation therapy. Neurologic signs in the remaining dog improved after treatment completion. During treatment, neurologic signs remained stable in 5 dogs. Fourteen dogs had improvement in behavior and gait. Blindness resolved in 1 dog. After irradiation, a stable period was observed in 20 dogs. Complete remission of neurologic signs was observed in 10 dogs, and a partial remission was observed in 10 dogs. Time to improvement of neurologic signs ranged from 9 to 35 days (median, 16 days) after the beginning of treatment.

A significant (P = 0.0012) correlation was found between severity of neurologic signs and RTS (Fig 3).
Figure 5—Plasma cortisol concentrations before and after megavoltage irradiation for treatment of pituitary macrotumors in 19 dogs. Plasma samples were obtained before and 1 hour after O ACTH stimulation. The symbol @ indicates dogs treated with mitotane. The hatched horizontal area represents the borderline range.

In dogs with grade-1 signs, RTS (mean ± SE, 8.0 ± 0.9%) was significantly smaller than that in dogs with grade-2 (15.0 ± 1.8%) or grade-3 (15.3 ± 1.0%) signs. A significant (P = 0.0017) correlation was found between remission of neurologic signs and RTS. Dogs with tumors with a small RTS (95% confidence interval, 6.65 to 10.54%) had a higher probability of achieving remission of neurologic signs than did dogs with larger tumors (Fig 4). Correlations were not found between remission of neurologic signs and tumor size, age, or sex. In dogs with PDH, correlations between neurologic status and duration of PDH and neurologic status and ACTH secretion were not found.

Figure 7—Relationship between relative tumor size < (— — —) or ≥ (— —) 12% and PFS rate in dogs with pituitary macrotumors treated with megavoltage irradiation.

Tumor recurrence was diagnosed by progression of clinical signs and increasing tumor size on radiographic examination using MRI (n = 3), CT (1), or at necropsy (7).

Endocrine response—In dogs with PDH, mitotane treatment was resumed if post-ACTH plasma cortisol concentrations were > 17 μg/dl to control the disease (Fig 5). Mitotane treatment was instituted within 8 weeks after irradiation in 3 of 12 dogs in which PDH was controlled by treatment with mitotane before irradiation, in 3 of 3 dogs in which PDH was not controlled by treatment with mitotane before irradiation, and in 1 of 4 dogs untreated before irradiation. The 2-year overall survival rate was 84% within 8 weeks of control of hypercortisolism after irradiation, 4 times was 90% and 2-year overall survival rate was 33% in dogs with recurrence of disease, although the difference was not statistically significant.

Analysis of overall survival and recurrence of disease indicated that a variety of neurologic signs at a survival time of 12 months, but not at a survival time of 6 months, predicts the likelihood of disease recurrence. Mean age at recurrence was 13.1 ± 8.8 months (range, 3-24). PFS was significantly lower in dogs with multivariate factors (P = 0.04) compared with those without factors (P = 0.0012). RTS ≥ 12% was associated with higher risk of recurrence (7). In dogs with grade-1 signs after ACTH stimulation, remission of neurologic signs was associated with endocrine disease recurrence (1).

Toxic side effects, particularly well tolerated. Case presentation included nausea, vomiting, and partial hearing loss. There were no deaths in the study period. Other evidence of disease was the presence of tumor invasiveness. The median survival time was 10.5 months (range, 5-24). There were 3 cases of stroke with moderate to severe neurologic deficits. These changes were not statistically significant. The median survival time was 10.5 months (range, 5-24). There were 3 cases of stroke with moderate to severe neurologic deficits. These changes were not statistically significant.
2-year control rate of hyperadrenocorticism was 32%. In the 12 dogs that were not treated with mitotane within 8 weeks after irradiation, mean duration of control of hyperadrenocorticism was 27.6 (± 7.9) months after irradiation. A difference in distribution of survival times was not found between dogs with ACTH stimulation test results above or within the reference range within 8 weeks after irradiation; 2-year survival rates were 33.3 (± 19.2) and 40.0% (± 19.8). Two dogs had recurrence of clinical signs of hyperadrenocorticism although the macrotumor decreased in size.

Analysis of survival—In the multivariate analysis of overall survival, the only diagnostic factor that significantly (P = 0.048) affected survival time was severity of neurologic signs. Mean and median overall survival times were 15.7 ± 2.9 months and 11.7 ± 5.9 months, respectively. Dogs with grade-3 neurologic signs had 6.6-times higher risk (P = 0.0116) for dying of disease than those with grade-1 neurologic signs. Mean and median PFS was 17 ± 3 months and 13.1 ± 8.3 months, respectively (Fig 6). For dogs with mild to moderate neurologic signs, mean and median PFS was 20 ± 3.5 and 21 ± 2.8 months, respectively. In multivariate analysis of PFS, significant diagnostic factors were RAS (P = 0.0038) and endocrine activity (P = 0.0401). Incremental increase in RAS was associated with a poorer prognosis. Dogs with tumors having RAS ≥ 12% had 4.1-times higher risk for progression than those with tumors having RAS < 12% (Fig 7). Dogs with endocrine-inactive macrotumors had 6.2-times higher risk for progression than dogs with PDH (Fig 8).

In dogs with PDH, plasma concentrations of cortisol after ACTH stimulation and of endogenous ACTH, pre-treatment with mitotane, duration of clinical signs, and endocrine response were not found to independently influence the overall survival or PFS (P > 0.05).

Toxicoses—Acute radiation reactions were generally well tolerated, self-limiting, and included epilation (n = 20) and otitis (4). Chronic radiation damage included hair depigmentation (n = 14) and deafness or partial hearing loss (2). Brain tissue in the radiation target volume examined at necropsy in 10 dogs had evidence of massive necrosis with hemorrhage of the tumor in 2 dogs, 1 of which had progressive neurologic signs during treatment and the other had died shortly after treatment completion. Of 7 dogs with recurrent neurologic signs (3 to 28 months after irradiation), necrosis of the pituitary stalk was found in 3. Sclerosis of the surrounding meninges was found in 2 dogs. Changes in white matter in the irradiated volume surrounding the tumor included diffuse areas of demyelination and reactive parenchymal gliosis. These changes were found in 3 dogs, in which the mean body weight was 20.3 kg (44.8 lb), that had been treated with 36 cm³ irradiation portal sizes, and in a 8-kg (17.6-lb) dog that had been treated with a 9-cm³ irradiation portal size. Vacuolation of optic and hypothalamic tracts was found in 1 dog. In 1 dog that had not had evidence of tumor progression (4 months after irradiation), there was complete sclerosis of the pituitary stalk and surrounding meninges but no evidence of tumor.

Discussion

Megavoltage irradiation was effective for treatment in dogs with neurologic signs attributable to pituitary macrotumors. Overall survival times of dogs in the study reported here were prolonged, compared with those for untreated dogs for which mean survival duration, once clinical signs developed, was 4.7 ± 2.0 months (range, 0.5 to 13 months), and for which 5 dogs had a clinical course of ≤ 2 months. In our study, survival duration was affected by severity of neurologic signs. Radiation therapy was effective in dogs with mild to moderate signs but did not improve survival in dogs with severe neurologic signs.

In our study, 4 of 5 dogs with deterioration of neurologic function during treatment died during or shortly after treatment. Deterioration of neurologic function in patients with brain tumors who are undergoing radiation therapy may result from tumor growth or necrosis or edema around the tumor.11 Death was directly related to extensive tumor necrosis and hemorrhage in 1 dog of the present report. Deterioration of neurologic function in the other 3 dogs that were not responsive to glucocorticoid treatment may have resulted from increased intracranial pressure attributable to tumor growth or from more severe peritumoral edema. Transient exacerbation of local neurologic signs after irradiation of brain tumors is not necessarily an indication that treatment has failed. These reactions may represent tumor response and self-limited localized reactions in white matter.13

The diversity of neurologic signs observed in dogs of this study can be explained by space-occupying effects of the tumor, resulting in selective loss of function within the thalamus, hypothalamus, and optic chiasma and in compression of temporal lobes.12 Although tumor size is an important factor affecting the response of pituitary tumors to treatment in people,1 results of our study confirmed those of a previous study1 that indicated that tumor volume was not a prognostic factor in dogs and confirmed that tumor size did not have value for predicting severity of neurologic signs.14 Severity of, and likelihood for, remission of neurologic signs after irradiation were affected by RAS (ie, size of tumor relative to calvarium size). This may be explained by the correlation found between tumor size and body weight and, thus, head size in dogs. For a given volume, a pituitary tumor is expected to induce more severe neurologic signs in a small dog than in a large dog, because small dogs have relatively smaller heads. Because brain volume is relatively constant in people, prognosis can be directly affected by tumor size.

In people, the role of irradiation for treatment of pituitary tumors is influenced by the tumor's histologic subtype. Patients with secretory tumors have a prolonged PFS, compared with those with nonsecretory tumors.16,17 In our study, dogs with ACTH-secreting tumors had a better prognosis than dogs with clinically endocrine-inactive tumors. A dose-response relationship has been demonstrated in people treated with primary radiotherapy who have large tumors that are causing mass effects and that are nonfunctioning adenomas but not those with corticotropic adenomas.18

This indicates that the prognosis for dogs with clinically endocrine-inactive tumors may be improved using an irradiation protocol in which a higher dose of radiation is given.

In dogs with PDH, pituitary irradiation was more effective in delaying tumor growth than in controlling ACTH secretion. Improvement of neurologic signs in our study was not contingent on a favorable endocrine response. The control rate of PDH in our study was comparable to results obtained in people with large invasive tumors. In people with adult-onset PDH, irradiation of the pituitary gland results in remission rates of 20% to 40%, using primary radiotherapy, and 55%, using radiotherapy in conjunction with adrenal blocking drugs. Irradiation appears to be more effective in children, who have a reported remission rate of 80%. In the present study, the true efficacy of radiation therapy for control of endocrine function may have been underestimated, because treatment with mitotane was instituted early (<8 weeks) after irradiation in some dogs. Because concentrations of circulating hormones may require several months to return to within the reference range after irradiation, some dogs may have been treated with mitotane before the full therapeutic response was obtained. Further, hypercortisolemia after treatment does not necessarily imply the persistence of disease. High plasma cortisol concentration has been suggested to be attributable to damage to the pituitary stalk by the tumor or the treatment. Evidence at necropsy of hypothalamic tumor invasion by tumor or hypothalamic damage after irradiation is consistent with these findings.

Relative tumor size was an indicator of endocrine status in dogs with PDH and neurologic signs before irradiation. However, RTS was not found to predict normalization of endocrine status in dogs treated with irradiation. A correlation between tumor size and endocrine status after irradiation was not found in this and other studies. Pituitary function in dogs with PDH does not necessarily decline rapidly after irradiation despite decreased tumor size. In our study, clinical and biochemical evidence of PDH was found in 3 dogs, although tumor size had decreased. In another dog, tumor increased in size without recurrence of PDH. However, these results should be interpreted cautiously because of the short follow-up period, slow normalization of ACTH plasma concentrations after irradiation, and sample variability in measurements of plasma concentrations of endogenous ACTH.

Acute or early delayed radiation complications in the brain were not observed. This is consistent with the apparent brain tolerance in dogs and people to dose fractions of up to 6 Gy, provided that total doses are appropriately reduced. In the 7 dogs that were evaluated after more than 12 months (survival range, 14 to 42 months), clinical expression of late radiation complications in the brain was not observed. Late radiation reactions of the brain include neurologic impairments, white matter necrosis, pituitary-hypothalamic dysfunction, and injury to cranial nerves. In dogs with tumor progression or recurrence, changes found in the pituitary stalk and surrounding brain tissue were a combination of radiation effect and tumor extension and compression. Because the site of injury was close to the tumor, pressure from tumor growth could not be eliminated as a cause for some of the changes observed in brain tissue surrounding the tumor. Evaluation of radiation damage may have been compounded by the increased susceptibility to brain injury observed in people with hypertension and those treated with mitotane and glucocorticoids. Although the dose-fractionation schedule may exceed the lower limits of tolerance, brain necrosis was not observed, because small treatment volumes may result in low incidence of chronic radiation complications. In our study, radiation damage including demyelination and reactive parenchymal gliosis were observed in dogs treated with treatment fields that were large, relative to head size. The poor results obtained in this study for tumors with a large volume relative to calvarium size and the substantial brain toxicity indicate that the protocol was not optimum. In people, radiation dose and fraction size are important determinants of endocrine dysfunction and brain damage after radiation therapy of the pituitary gland. A dose per fraction of ≤2 Gy and a total dose of ≤55 Gy may result in low incidence of radiation complications in the brain. Most reports of radiation necrosis in people are associated with fractions >2.2 to 2.5 Gy. For treatment of large pituitary tumors in dogs with neurologic signs, use of a higher radiation dose and smaller dose fractions (approach 2 Gy) may improve long-term survival and decrease the risk of radiation toxicities.

Results of this study support previous findings that radiation therapy is effective for dogs with pituitary macroadenomas with mild to moderate neurologic signs. Treatment protraction appears to negatively affect efficacy. With a total dose of 40 Gy given in 4 Gy/fraction during 3.5 weeks, mean and median survival of dogs with mild neurologic signs were 24.6 and 24.7 months, respectively. With a protracted protocol (ie, 54 Gy given in 3 Gy/fraction during 6 weeks), dogs with similar neurologic signs had a shorter mean (5.3 ± 8.6 months) and median (2.5 months) survival time. Lengthening overall treatment time to lessen acute effects and increase tumor dose may not be optimal for treatment of pituitary tumors in dogs. Benefits of higher dose may be lost when overall treatment is increased because of the phenomenon of accelerated tumor repopulation.


