

# New Treatment Modalities for Brain Tumors in Dogs and Cats



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## KEYWORDS

- Canine • Central nervous system • Convection-enhanced delivery • Feline • Glioma
- Immunotherapy • Oncology • Radiotherapy

## KEY POINTS

- Advancements in magnetic resonance (MRI) and functional neuroimaging will continue to improve the clinical management of brain tumors.
- Stereotactic radiosurgery (SRS) is emerging as a viable treatment of many canine and feline brain tumors and can be performed with minimal toxicity using dedicated radiosurgical units or contemporary linear accelerators.
- Convection-enhanced delivery (CED) is a promising therapeutic platform that bypasses the blood-brain barrier (BBB), allowing for direct administration of macromolecular anti-neoplastic agents to brain tumors.
- CED is used to treat dogs with spontaneous brain tumors but consistent and accurate delivery of drugs remains a challenge to mainstream clinical adoption of this technique.
- Advancements in neuroimmunology and tumor biology have led to the development and clinical translation of several novel immunotherapies with therapeutic potential in canine and human brain tumors.

## INTRODUCTION

Transformative advances in MRI over the past 3 decades allow for the detailed neuro-anatomic characterization and presumptive antemortem diagnosis of many canine and feline brain tumors.<sup>1–4</sup> MRI has also served as a fundamental platform for the development of technologies and procedures that have contributed to improvements in the management of brain tumors, including image-guided neuronavigation, functional neuroimaging, surgical and radiotherapeutic planning, and objective therapeutic response assessment.<sup>5–9</sup> Despite this progress, definitive antemortem diagnosis of brain tumors in animals remains uncommon, and few data exist in veterinary medicine

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regarding the influence of treatment on clinical outcomes of animals with brain tumors. Primary brain tumors, in particular the malignant variants, remain a source of significant morbidity and mortality in small animals and humans.<sup>10,11</sup>

### ***Current Therapeutic Options***

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The prognosis for dogs with palliatively-treated brain tumors is poor. In one study of dogs with brain tumors definitively diagnosed at necropsy, the reported overall median survival was approximately 2 months after diagnosis via brain imaging.<sup>10</sup> Surgical resection and fractionated radiotherapy are currently the principal methods used to treat canine and feline brain tumors, and these therapies are capable of improving both the quality and quantity of life in small animals. However, both surgery and radiotherapy can be associated with treatment-associated morbidity, and local treatment failures after these therapies remain a common cause of death or euthanasia.<sup>12–17</sup> Surgical treatment has been best described for forebrain meningiomas, which is the most common primary brain tumor type in both dogs and cats.<sup>8,12–15</sup> In dogs with meningiomas, the reported median survival after traditional surgical resection is approximately 7 months.<sup>12</sup> In cats, the median survival after surgical resection of forebrain meningiomas is 24 months.<sup>13,14</sup> Neurosurgical treatment that incorporates devices that improve intraoperative visualization, such as intracranial endoscopy, or facilitate tumor extirpation have been associated with median survivals ranging from 42 to 70 months.<sup>8,15</sup> Transsphenoidal hypophysectomy has been demonstrated to be an effective surgical technique in dogs and cats with nonenlarged to moderately enlarged pituitary adenomas, with a reported 4-year survival rate of 68% in dogs.<sup>16</sup> Currently available surgical techniques often preclude safe resection of intraparenchymal tumors that are infiltrating the surrounding brain or intimately associated with critical neuroanatomic structures. There is little information available regarding the efficacy of or indications for surgery in canine and feline brain tumors other than meningiomas and pituitary tumors.

Fractionated radiotherapy is beneficial in the treatment of brain tumors as a sole therapeutic modality or as an adjuvant after surgery.<sup>12–18</sup> Studies investigating treatment of a variety of presumptively diagnosed brain tumors in dogs with fractionated radiotherapy reported median survivals that range from approximately 300 to 700 days.<sup>17,18</sup> Dogs with meningiomas treated with 3-D conformal radiation therapy had an overall median survival of 577 days, and the median survival increased to nearly 30 months (ie, approximately 900 days) when dogs dying of causes other than meningioma were excluded.<sup>19</sup> Systemically administered cytotoxic chemotherapeutics, including those agents capable of penetrating BBB, are largely ineffective as sole agents for the treatment of brain tumors. A recent study failed to demonstrate any difference in survival between dogs with brain tumors treated symptomatically with prednisone and anticonvulsant drugs compared with those that received symptomatic therapy and lomustine.<sup>20</sup>

There is increasing recognition of the epidemiologic, neuropathologic, molecular, and genetic homologies between canine and human brain tumors, which has driven the use of dogs with spontaneous brain tumors as a translational disease model.<sup>21–23</sup> This review introduces contemporary therapeutic advancements for brain tumors and illustrates the role that tumor-bearing dogs have made to progressing the field of translational neuro-oncology. Because an exhaustive survey of brain tumor treatment is beyond the scope of this article, it focuses on SRS, CED, and immunotherapy (IT). These therapies hold great promise for the treatment of brain tumors and are being used clinically in dogs and cats.<sup>23–25</sup> Reviews of boron neutron capture therapy, brachytherapy, high-intensity focused ultrasound (HiFU), gene therapy, laser

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