What is Radiation Therapy?

Gliomas or malignant tumors found deep within the brain tissue are the second most common brain tumors in dogs[1] and are especially hard to treat. A presumptive diagnosis of a brain tumor has been made in your dog based on the clinical signs, such as seizures or circling, and an MRI. Because gliomas tend to invade normal tissue, surgical removal of tumors is difficult and seldom curative. Thus, radiation therapy frequently combined with chemotherapy is often the only viable treatment options in pets.

Radiation therapy (RT) uses beams of intense energy to kill cancer cells. Typically, we use intensity modulated radiation therapy (IMRT) where the radiation is divided into smaller doses called "fractions," which are given Monday-Friday until the total dose is achieved. Prior to radiation treatment a "mask" is made of your dog's head to allow precise positioning of your dog for each radiation therapy treatment. A planning computed tomography (CT) is obtained when the mask is made and will be used by the radiation oncologist to target the radiation to the tumor and try to avoid normal tissue that could cause unwanted side effects. Because your dog must remain very still for treatment, the mask, planning CT, and radiation fractions are performed with your dog under general anesthesia. The goal of radiation therapy is to stop the growth of your dog's brain tumor or even cause it to shrink.

How long does a treatment take?

The mask and planning CT take about an hour and is performed typically the week prior to treatment. Each IMRT session only lasts 5-10 minutes. However, the RT fractions are performed under general anesthesia and positioning your dog exactly right for treatment are of the utmost importance. Also, since your dog has a brain tumor, special medications may be administered to reduce potential brain swelling and recovery from anesthesia may be slower than in a healthy dog. Should the veterinary anesthesiologist assess the patient and decide your dog should not receive further anesthesia for the day, the RT will be delayed or re-scheduled.

What are the benefits of radiation therapy and how long will it take to see them?

While survival time will vary based on the type of tumor, location, and size, the median survival time for dogs after receiving RT with gliomas is 12-15 months.[2] The median survival time with palliative medical treatment, e.g., corticosteroids, alone is ~1-2 months.[2]

You may see a response to the radiation therapy in as short a time as a week as the mass shrinks and creates less pressure on the surrounding normal tissue. The full effects of IMRT may take weeks to months. However, we recommend that even if your pet is improving that you continue to administer anti-seizure medications that are recommended by your veterinary neurologists.

What type of chemotherapy will my pet receive?

Temozolomide (TMZ) is a chemotherapeutic agent which is a standard component of treatment of human patients with both newly diagnosed and recurrent anaplastic astrocytoma (AA) or glioblastoma multiforme (GBM) brain tumors. TMZ when combined with surgery and RT has shown a survival benefit in human patients. However, RT plus TMZ, while well tolerated in the dog, has not been performed in enough dogs with suspected gliomas to determine whether this

same survival benefit occurs in pets.[3] RT plus TMZ will be compared to new therapies in another arm of this clinical trial.

How is TMZ given?

Temozolomide (TMZ) is given by mouth as a pill. TMZ will be given on the same days as radiation therapy. TMZ is generally well-tolerated in dogs. We will give you medications that can be given by mouth to help prevent any nausea from the TMZ.

How frequently will I need to come to the Center for Image-Guided Animal Therapy (CIGAT)?

You will need to come to CIGAT at least eight times of which five times are for Radiation Therapy and three times are for follow-up MRIs. Additional visits can be potentially coordinated with your regular veterinarian or neurologist. The expected number of visits is as follows:

1. Enrollment visit including a neurological examination prior to radiation therapy. (May not be required depending on referral from neurologist.)
2. Visit for CT planning and mask.
3. Radiation therapy will be given on five consecutive weekdays. We do not perform RT on the weekends.
4. Post-chemotherapy bloodwork at ~1 week. This visit can potentially be performed at your local veterinarian.
5. Follow-up MRIs at 3, 6, and12 months after radiation treatment.
6. We also recommend that you have a neurologist who you can call for follow-up care in between treatments.

What happens if my pet has an emergency after treatment?

If you think your pet is seriously ill and needs immediate medical attention, you should go to your local emergency hospital or daytime veterinary hospital.

If you are not sure if you have an emergency, you may choose to call the Center for Image-Guided Animal Therapy (410) 502-7325 and leave a message (messages are checked at the beginning and end of the day Monday through Friday) or preferably send an email (cigat@jhmi.edu) that will be read daily.

How do I prepare my dog for the procedure?

1. Your dog should not eat after midnight, the evening prior to the IMRT. Water is fine.
2. All collars, identification tags, hair clips, and pet clothing will be removed prior to the procedure.

What should I expect after the procedure?

After each IMRT fraction, barring any significant complications, you should be able to bring your dog home. Otherwise, your dog will be monitored overnight in the ICU and returned to you after the next treatment.

After you complete your radiation therapy, you should continue to monitor your dog's progress at home. One-week after the procedure, we will perform a blood draw to look for potential bone marrow suppression from the TMZ. You should also see your neurologist monthly for follow-up

visits. Three months after the IMRT, we will perform an MRI at the Center for Image-Guided Animal Therapy; there is no charge for this scan. We will also typically repeat the MRI at 6 months and again at 1 year after treatment.

Lastly, as it is vital to the study that we thoroughly investigate how radiation therapy and TMZ affects your dog, we request that you allow us to perform a necropsy on your dog upon his/her natural death. Furthermore, because the MRI cannot determine the type or grade of the tumor we are treating, this can only be determined by microscopic evaluation of the mass. Upon completion of the necropsy, we would arrange for a private cremation for your dog should you desire it, for a small fee, and you would receive your dog's ashes. While it is important to perform the necropsy to understand how the treatment affected your dog, we understand if you would like to opt out of this portion of the study. Opting out of the necropsy will not affect your dog's treatment in the study.

References

1. Snyder JM, Shofer FS, Van Winkle TJ and Massicotte C. Canine intracranial primary neoplasia: 173 cases (1986-2003). *Journal of Veterinary Internal Medicine*. 2006;20:669-75 http://www.ncbi.nlm.nih.gov/pubmed/16734106.

2. Moirano SJ, Dewey CW, Wright KZ and Cohen PW. Survival times in dogs with presumptive intracranial gliomas treated with oral lomustine: A comparative retrospective study (2008-2017). *Veterinary and Comparative Oncology*. 2018;16:459-466

3. Dolera M, Malfassi L, Bianchi C, Carrara N, Finesso S, Marcarini S, Mazza G, Pavesi S, Sala M and Urso G. Frameless stereotactic radiotherapy alone and combined with temozolomide for presumed canine gliomas. *Veterinary and Comparative Oncology*. 2018;16:90-101 https://onlinelibrary.wiley.com/doi/abs/10.1111/vco.12316.