

Radiation Therapy – Side Effects

Adverse Radiation Effects (ARE)

Radiation therapy can be an effective method for treating tumors in pet animals. As in any type of cancer therapy, there are certain risks and side effects associated with treatment. Fortunately, radiation therapy is a regional rather than whole-body therapy in the majority of cases, meaning that the side effects are limited to the area of the body being treated for the tumor.

Radiation effects are classified as *early* or *late*. *Early* effects are seen during or shortly after radiation treatment, usually 2 weeks after starting radiation and continuing for about 2 weeks after radiation therapy is completed. Early effects occur in tissues that are rapidly growing, such as skin and the mucous membranes of the oral and nasal cavities. These effects can be uncomfortable to the patient and a concern to the veterinarian and owner, but they heal with time, usually in 3-4 weeks if uncomplicated. During this time, we will treat patients aggressively with medications to control discomfort and offer strategies to prevent self-trauma (E-collars, etc.)

Late effects of radiation occur in tissues that have slowly or non-dividing cells, such as the brain, spinal cord, heart, and bone. Late effects from radiation generally occur no sooner than six months following treatment but may appear years later. Late effects can be serious, even life-threatening, and they generally do not improve once they occur. The dose of radiation that is administered is tailored to the area being treated so the risk of serious late effects is less than 5% (1% for brain and spinal cord). For patients who live years following treatment, tumor formation secondary to radiation is possible. In order to be considered a radiation-induced tumor, it must be within (or very close to) the radiation field treated, is not a recurrence of the treated tumor, and is occurring at least 6 months after radiation, but usually longer. Radiation-induced tumors in veterinary medicine are extremely rare.

Your clinician will indicate which of the following radiation effects are likely to affect your pet.

Skin

If your pet has a tumor located in the skin or just below the skin surface, or a surgical scar harboring microscopic tumor cells, radiation effects to the skin will develop if treated with a full-course, fractionated protocol.

Redness to the skin can occur around the second week of treatment. This is followed by ulceration of the skin surface, known as *moist desquamation*. This is irritating to your pet, and most animals will try to lick and scratch at the area. It is VERY important to prevent self-trauma with an Elizabethan collar (E-collar) as this increases the risk of delayed healing and infection. The skin reactions will get worse through the end of radiation therapy and may be most severe AFTER radiation therapy is completed. In some animals, skin effects do not begin to develop until radiation therapy is done. The skin will heal in the 2-4 weeks after the effects are at their worst if there are no complications (infection, steroid usage, and certain systemic diseases). The skin may continue to be thinner or thicker than normal, and the skin pigment may be darker or lighter than normal.

Do NOT apply petroleum-based ointments to the skin. Animals tend to lick ointments off, and this can contribute to the severity of early effects. Ointments left on during the radiation treatment can also make effects worse. Consult with your oncologist before applying ANY topical treatments to radiation sites. If side effects are severe or markedly painful, your radiation oncologist may prescribe a specific topical agent to be administered at home, or may recommend recheck exams and side effect treatment while your pet is anesthetized.

The hair in and around the radiation field may be shaved to mark the radiation field and to allow close monitoring for side effects. If the hair is not shaved, it will usually fall out during the third week of treatment. Hair will usually

regrow in 3-6 months, but this may vary with the seasonal coat growth seen in some breeds of dogs and cats. The hair can grow back in a different color or texture. In some patients, the hair loss in the radiation field is permanent.

Cats are generally more resistant to radiation effects of the skin. Most cats will have hair loss and dry flaking of the skin which may itch. It is still important to prevent your cat from further irritating the area (E-collar).

Lymphedema

A small percentage of patients who have radiation around the entire circumference of a limb can develop swelling and edema of the limb distal (or farther away from the body) to the radiation field. This occurs many weeks to a few months after treatment. Radiation can damage the vessels, called lymphatics, which clean up any liquid that leaks out of blood vessels. If these vessels are damaged, fluid builds up in the tissues and looks like swelling. This can cause increased pressure in the limb and discomfort for the patient. The treatment for this swelling, called *lymphedema*, is physical therapy and pain medications. Notify your radiation oncologist if you notice persistent, uncomfortable swelling in your pet's limb.

Oral Cavity (Mouth)

Side effects to the oral cavity may develop in patients that have a tumor located in the upper or lower jaw (maxilla or mandible), hard or soft palate inside the mouth, and in patients with tumors in the nasal cavity. Depending on the location of the tumor, some patients with brain tumors or tumors of the skull may develop radiation side effects to the oral cavity.

The mucous membranes of the mouth can become reddened and swollen, known as *mucositis*. The surface of the mucous membranes can become ulcerated and form a yellow-gray plaque. The saliva may appear "ropy" and thicker than normal, and salivation is often profuse. There is often a foul odor from the mouth (halitosis).

Some animals will continue to eat well through their treatment, but many do not eat enough due to the discomfort associated with mucositis. Human radiation therapy patients report a decrease in taste acuity, and this likely occurs in our veterinary patients, especially if the tongue is in the treatment field. Commercial foods with high levels of salt may be irritating. Try a variety of foods to find something your pet will find palatable. Cooked chicken breast, hamburger, turkey, hot dogs cut into pieces and rice or baby food (WITHOUT onion or garlic in the ingredients) have all been used successfully. Some patients prefer to have the food blended into gruel while others respond better to small "meatball" shaped pieces that can be swallowed whole. Coaxing your pet to eat by hand feeding helps encourage some patients to eat, and some patients may prefer food that is warmed up.

Maintaining proper hydration and nutrition is very important during any type of cancer treatment. If your pet is not able to eat and drink a sufficient amount during radiation therapy, it may become necessary to place a temporary feeding tube into the esophagus or stomach. Dogs and cats tolerate these feeding tubes very well. Your clinician will discuss this with you if it is likely to be necessary for your pet. A consultation with a veterinary nutritionist may also be recommended if special or home fed diets are desired.

Nasal Cavity (Nose)

The nasal cavity is lined by mucous membranes which can be affected similarly to the oral cavity. Most pets with a nasal tumor have some nasal discharge before radiation therapy begins. This discharge may initially get worse following or even during treatment, and may range in color from clear to white to slightly yellow, and it may be blood tinged from the tumor. The discharge will improve 2-4 weeks after radiation therapy is completed, but because of the damage that the tumor has done to the normal structures of the nasal cavity, it may not resolve completely. In addition, the defenses of the nasal cavity will never be completely normal again due to disruption of the tissue by the tumor and radiation damage to the normal mucosa. Months to years after treatment, our radiation patients are more prone to bacterial, or rarely fungal, infections of the nasal cavity (chronic rhinitis). If there is an increase in discharge or change in the color (especially to yellow or greenish) please seek veterinary care as antibiotics or diagnostics may be warranted. Sneezing, reverse sneezing, intermittent coughing or congested breathing usually improve after radiation therapy, but in some patients or with certain tumor types, these clinical signs may never fully resolve.

Esophagus and Trachea

Side effects to the esophagus and trachea can occur in pets that have a tumor located in the neck or the chest. The trachea is the windpipe in dogs, and the esophagus is the organ that connects the mouth to the stomach. Both organs are lined with mucosa, which is sensitive to acute radiation side effects. These mucous membranes can become reddened and swollen, known as mucositis. For these organs, that would present as dry, hacking cough, decreased appetite, vomiting/regurgitation after eating and/or exaggerated or painful swallowing. You might also notice excessive salivation if a pet has painful swallowing and doesn't want to swallow its saliva. Late side effects to these organs are rare and would include scar tissue formation in the area. While the trachea has rigid rings to hold its shape, the esophagus has no structure, and scar tissue could narrow the opening of the esophagus. This could make swallowing solid foods difficult or, in severe cases, impossible. This scar tissue formation occurs over many months to years after therapy. Even more rarely, if acute side effects to the esophagus are severe, perforations (or holes) in the wall of the esophagus have been reported in people. This is an emergency situation.

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Eyes

When treating nasal, oral or brain tumors, one or both eyes may be in the radiation field. We avoid irradiating the eyes whenever possible, but it is often unavoidable due to the location of the tumor. The superficial layers of the eye and inner eyelid can become irritated, red, and inflamed (keratitis, conjunctivitis). In addition, the tear glands are sensitive to radiation, and may decrease or stop producing tears causing a condition known as keratoconjunctivitis sicca (KCS) or "dry eye". This may or may not be permanent, depending on your pet's sensitivity to radiation, and can start as early as 2 weeks following treatment or as late as 6 weeks. It is essential to treat the eye with artificial tears to keep the cornea moist, or the cornea will become damaged. Taking good care of the cornea is important for maintaining long term vision.

The lenses of the eye are also sensitive to radiation. An eye that is in the radiation field may develop a cataract 6-12 months following radiation therapy. The pet may become blind in that eye due to the cataract, or may retain some vision. The radiation oncologist will typically attempt to spare one eye more than the other if possible, so the pet can remain visual enough for daily activity. If blindness is affecting your pet's quality of life, cataract surgery can correct the blindness in most patients. Many blind dogs can learn to adapt to their environments and retain a good quality of life. Consult your veterinarian for resources on supporting your blind dog at home if needed.

We recommend having a consultation with an ophthalmologist for a full eye exam prior to radiation therapy in the head and neck region. This gives us a baseline to monitor for any radiation effects, and often reveals subclinical or mildly clinical conditions. Recheck eye exams may be recommended based on any initial findings or the clinical presentation of the patient. At the very least, tear production tests should be performed prior to radiation, 2 weeks after, and 4-6 weeks after radiation of high-risk patients.

Ears

When treating tumors of the brain or skull, one or both ears may be in the treatment field. The epithelial lining of the ear canal is subject to the same irritation as the skin, and the ear canals can become reddened or ulcerated.

Ear discharge may be noted. Some owners report that their pets do not hear well following radiation therapy. The exact cause of hearing loss is not well understood. It may be the result of permanent damage to the fine hairs in the ear canal or the result of chronic build-up of shed skin cells and discharge. Your clinician may recommend a hearing evaluation prior to the start of radiation therapy. Ear drops may be dispensed to help minimize the irritation to the ear canal. Consult your physician before starting any ear drops during radiation therapy as this could exacerbate side effects to the ear canal in the short term. Some animals have chronic ear problems (scratching or rubbing the ears) after radiation therapy. Rarely a patient will develop a head tilt or balance disorder from changes to the inner ear. This may be a temporary problem, or, rarely, a permanent issue.

Brain and Spinal Cord

Patients with nasal or oral tumors can sometimes have small portions of the brain in the radiation field. Unless the pet presents with neurologic signs, it is very uncommon for radiation to cause neurologic abnormalities in these patients. If they do occur, they are typically >6 months after radiation. Patients being treated for brain tumors are at higher risk of side effects to the brain. They are usually divided into *acute*, *acute delayed*, and *late effects*.

Acute effects can occur immediately following treatment up to two weeks after treatment. This is most often related to the anesthesia associated with radiation treatment, as some anesthetic medications can increase the pressure inside the skull leading to neurologic side effects. There is also a risk of radiation-induced inflammation of the normal brain tissue surrounding tumors and this can lead to anything from mild dullness and sensitivity to light all the way to seizures and becoming non-responsive in severe cases. There is a small risk of death in this short term, usually in pets with very large tumors or who were already very debilitated before starting treatment. Our anesthesia service and technicians are always well informed about patients with brain tumors and take every precaution to mitigate these risks as much as possible. Intervention with medications or even sometimes hospitalization is recommended on a case-by-case basis.

Acute delayed effects occur in about 10-30% of patients receiving radiation for brain tumors and can happen 2-6 months after radiation therapy. We suspect they are related to swelling (or edema) and inflammation of the brain or spinal cord secondary to radiation and/or dying cancer cells. This may present as an acute worsening of neurologic signs. The vast majority of patients with acute delayed effects are responsive to steroids, and restarting or increasing the dose of this medication may be recommended. These changes are usually temporary, but it may be months before a recovery is made. In uncommon cases, hospitalization on IV medications may be recommended. Recurrence of the tumor during this time period following radiation is very unlikely, however possible with aggressive brain tumors.

Late effects to the brain and spinal cord are rarely seen prior to 6 months after the completion of treatment but can occur years later. Depending on the portion of the spinal cord treated, the patient may have decreased ability to move the hind or front limbs or may even become completely paralyzed. In the case of late effects from brain irradiation, the patient may have decreased awareness, change in attitude or behavior, seizures or other neurologic signs. The vast majority of cells in the brain do not divide and/or grow in adults. Cells that are damaged or killed generally cannot be replaced. Therefore, late effects to the brain can be serious or life-threatening. *For this reason, the radiation oncologist is careful to keep the risk of late effects to the brain and spinal cord as low as possible, however this risk is never zero.*

Patients being treated for brain tumors may or may not improve clinically during radiation therapy. While some patients improve dramatically during radiation therapy, some may get worse during treatment. Your clinician can give you more information on your pet's suspected individual risk for these side effects.

Lungs

A portion of the lung may be included when a tumor is located on the body wall or within the chest cavity (thorax). The lungs are very sensitive to damage by radiation therapy. This damage occurs in two phases. The first phase, called pneumonitis (inflammation of the lung), occurs 2-6 months after treatment. Most animals show no symptoms of pneumonitis, although it can be seen on a chest x-ray. Some patients will have a cough, and a few may have some difficulty breathing. Pneumonitis is usually temporary and can usually be treated with medication if necessary.

The second phase of damage is related to scarring of the lung tissue (fibrosis). Even very low doses of radiation therapy can lead to scarring (fibrosis) of the lung 9-12 months after radiation therapy, and the irradiated lung will not be functional. Your radiation oncologist is very aware of the volume of lung included in the treatment field and will make treatment recommendations with the goal of keeping lung fibrosis to a minimum. Almost all dogs and cats will have an excellent quality of life with 2/3 to 1/2 of their normal lung volume. There will be permanent changes to the lungs visible on the patient's chest x-rays. It is important for your veterinarian to know that your pet has received radiation in the past so that these changes are not diagnosed as severe pathology.

Colon and Bladder

A portion of the colon, rectum and bladder are often in the treatment field when treating tumors near the pelvis. The lining of these organs is made up of rapidly dividing cells similar to the skin and oral cavity. Irritation of the colon (colitis) may develop near the end of the second week of treatment and may continue for 2-4 weeks after radiation is completed. You may see diarrhea which may contain mucous and/or small amounts of fresh blood. Your pet may defecate small amounts more frequently. Some patients have intermittent colitis long term. Inflammation of the bladder (cystitis) can also occur and follows the same timeline. Clinical signs of cystitis are straining to urinate, blood in the urine, or increased urgency to urinate (asking to go outside many times during the day or accidents inside the house). Your clinician may recommend medication or dietary changes to help alleviate the problem.

Any diarrhea seen immediately following the start of radiation therapy (within 1-3 days) is not related to radiation, but rather to stress from hospitalization. This colitis is treated with oral medication in most cases and may resolve during the course of therapy as the patient becomes accustomed to the radiation routine. If anxiety and stress are persistent, this diarrhea may not completely resolve until therapy is completed.

Late side effects are rare but can develop in these areas as well. They occur many months after radiation and are related to scar tissue formation. Scar tissue in the colon may not be a problem if only a section of the colon or rectal wall is involved. If scar tissue forms circumferentially around the colon, this could result in a stricture, resulting in difficulty passing stools. Urinary strictures secondary to scar tissue formation are also possible, which could result in long-term straining to urinate. If the scar tissue completely obstructs the flow of urine, this is an emergency. There are sometimes procedures that can be performed to alleviate a rectal stricture ("ballooning" or stent placement). Stents can be placed in the urethra to reestablish urine flow, however this usually makes the patient incontinent. Fistula formation (holes forming in the walls of the colon, rectum or urethra) secondary to radiation are exceedingly rare, but, when they do occur, are life-threatening.

Abdominal Radiation – Cats

About 60% of cats who proceed with this abdominal radiation protocol will experience some degree of gastrointestinal upset (vomiting, diarrhea, decreased appetite), however these clinical signs are generally mild and transient in the majority of patients. About 50% of cats will develop changes to their blood cell counts during or for several weeks after radiation, so periodic blood work rechecks are recommended. The kidneys and the liver may also experience toxicity from the radiation. With this protocol, few if any cats develop clinical signs related to liver damage, however we may notice elevations of liver enzymes on bloodwork moving forward. Probably more concerning for cats is the possible toxicity to the kidneys. Older cats tend to have a high rate of chronic kidney insufficiency or disease, and radiation can accelerate or exacerbate the natural tendency. We administer fluids, either intravenously or under the skin, on each day of radiation treatment to our cat patients as long as they do not also have heart disease. This is to help support the kidneys during anesthesia and radiation. Periodic blood work will also be used over the next several weeks to months to monitor for any long-term effects the radiation may have had on your pet's kidneys.

Small Intestines

The lining of the small intestines is made up of rapidly dividing cells similar to the skin and oral cavity. Irritation of the small intestines (enteritis) may develop near the end of the second week of treatment and may continue for 2-4 weeks after radiation is completed. You may see diarrhea which may be watery, and your pet may defecate small amounts more frequently. Your clinician may recommend medication or dietary changes to help alleviate the problem.

Any diarrhea seen immediately following the start of radiation therapy (within 1-3 days) is not related to radiation, but rather to stress from hospitalization. This enteritis is treated with oral medication in most cases and may resolve during the course of therapy as the patient becomes accustomed to the radiation routine. If anxiety and stress are persistent, this diarrhea may not completely resolve until therapy is completed.

Late side effects are rare but can develop in these areas as well. They occur many months after radiation and are related to scar tissue formation. If your pet ever receives abdominal surgery in the future, they may notice increased adhesions (organs sticking together) between the intestines and the body wall. Fistula formation (holes forming in the walls of the small intestines) secondary to radiation are exceedingly rare, but, when they do occur, they are life-threatening.

Veterinary Specialty Center is guided by the belief that companion animals deserve state-of-the-art medical care in a kind and comforting environment. The courage of our patients, the loyalty of their human families, and the devotion of our referral veterinarians inspire our vision. It is sustained by the contributions of our compassionate, knowledgeable and dedicated staff and built upon a tradition of providing unsurpassed healthcare for animals.
