

O - Oncology

RADIATION THERAPY FOR BEGINNERS

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Radiation is becoming widely available to treat tumors in veterinary patients. Orthovoltage machines capable of delivering low energy external beam radiation are less versatile than linear accelerators and cobalt-60 machines that deliver megavoltage radiation. In addition, electron beam capabilities that are available with some linear accelerators allow more targeted treatment in our smaller patients. With the increased availability of computerized treatment planning, and the delineation of the extent of the disease by CT and MRI, the beneficial effects of radiation therapy are bound to increase substantially. The future of radiation therapy will be tied into the use of radiobiological and tumor biology information to enhance the beneficial effects of radiation therapy. In addition, the combination of radiation therapy with surgery and chemotherapy may result in substantial improvement in the efficacy of this treatment modality.

PALLIATIVE OR DEFINITIVE RADIATION THERAPY

One of the most important decisions is whether a patient should be treated with curative or palliative intent. This influences not only the course of treatment, but expectations of the caregiver for their pet.

Treatment with curative intent (definitive therapy) is often complicated, requiring frequent travel and multiple anesthetics. The total dose of radiation is usually higher than are required for palliation and consequently the risks of unfavorable sequelae are greater. Such treatment is likely to be prolonged and expensive; however, for many tumors the chance of long-term tumor-free survival (> 3 years) is high.

Palliative radiation therapy should have a specific and often short-term goal, usually to relieve pain or symptoms of cancer. It is often performed when a specific site is causing a problem to the patient, but the rest of the cancer is unlikely to respond to any treatment (e.g. a painful digital metastasis

from a pulmonary tumor that is not causing signs at any other site). For this reason, palliative therapy should minimize cost, inconvenience, discomfort and risk of side effects, and should be completed in the shortest reasonable time.

TIMING OF RADIATION THERAPY

Radiation is most effective at the periphery of a tumor where there are small numbers of cells that are well vascularized. In contrast, surgery is limited by preservation of normal tissues adjacent to the tumor and therefore fails microscopically and peripherally due to residual tumor cells. Surgery and radiation therapy are therefore complementary.

Most radiation therapy in veterinary practice is delivered postoperatively to the residual microscopic tumor. **Postoperative (adjuvant)** radiation therapy has the advantage that it is possible to histologically identify patients with residual disease that would benefit most from radiation therapy. The major disadvantage is that surgery may reduce tumor vascular supply. Tumor cells along the surgical scar may survive radiation therapy because they are protected in a relatively hypoxic environment. In addition, a large surgical scar will increase the size of the radiation field and hence the risk of side effects.

One study evaluated the effect of starting radiation therapy the day after surgery compared to delaying until 1 or 3 weeks after surgery. They found that the strength of tissues was significantly less when radiation started immediately after surgery, but healing was unaffected when the delay was 1 week or longer.

Preoperative (neoadjuvant) radiation therapy has the advantage of sterilizing well-oxygenated cells at the periphery of a tumor before the vascular supply to these cells is compromised by surgery. Cells in the periphery that could be dislodged and seeded at the time of surgery are also irradiated. Preoperative radiation therapy may also reduce tumor volume in unresectable

tumors but this should not be used as a reason to reduce the size of the surgical field any more than is absolutely necessary to preserve normal structures. Disadvantages of preoperative radiation therapy include a delay of surgery while acute effects resolve, however, if peripheral cells are sterilized, this wait is not compromising the patient. A reduction in gross tumor size may lull the surgeon into attempting a less aggressive surgery. Another potential disadvantage is that fatally irradiated tumor cells may not die until they attempt mitosis, which can make histologic interpretation of surgical margins difficult.

Whether radiation is used preoperatively or postoperatively, irradiation of a large volume of tissue leads to a poor outcome. When large areas are irradiated, planning is made more difficult and a larger volume of normal tissue is irradiated. This leads to a decreased chance of tumor control and an increased risk of complications. The earlier in the course of cancer that radiation is used, the more likely it is to result in a successful outcome and the less likely it is to result in severe toxicity.

CLINICAL OUTCOMES

When comparing results from veterinary studies that use radiation therapy, the reader should note not only the median survival times and tumor control rates but also long-term survival rates as well as acute and late complication rates. The low total doses used in early veterinary studies meant that with few exceptions long-term tumor control was rare, survival was short and therefore late effects of radiation were rarely seen. The treatment schedule was determined by the difficulties of repeated anesthesia, rather than by radiobiological necessity and reported acute effects are relatively mild and short lived. More recently, safe short-acting anesthetics have allowed more frequent treatments with smaller doses per fraction, and the ability to deliver higher total doses has increased as fraction size has decreased. The recent radiation therapy literature is certainly more encouraging to veterinary practitioners.

Oral Tumors

The most common oral tumors in dogs are malignant melanoma, squamous cell carcinoma, fibrosarcoma, and epulides. Radiation therapy is effective for local control of many of these oral tumors.

Nasal Tumors

There is little doubt that radiation therapy is the treatment of choice for dogs with nasal tumors. There is much variation within the literature regarding response to therapy. The prognostic

factors that may influence response to therapy include tumor histology, clinical stage, tumor size, the type of radiation therapy, and the dose of energy delivered, as well as whether surgery was performed prior to radiation therapy.

Soft Tissue Sarcomas

Soft tissue sarcomas frequently recur after incomplete surgical excision because they have many “fingers” that extend out into surrounding tissues. Often, the tumor is excised only around the area that can be palpated, which ensures that disease will recur. Soft tissue sarcomas (STS) have been considered to be radiation resistant however higher total dosages provide long-term control of this tumor in the majority of dogs.

Mast Cell Tumors

Long-term control is likely for dogs with incompletely excised grade II mast cell tumors following radiation therapy. Approximately 90% of dogs with this tumor treated to a total dose of 48 to 54 Gy in 3 or 4 Gy fractions given three times a week postoperatively were still alive and tumor free three years after radiation. This treatment is clearly the choice for this tumor regardless of the protocol.

Brain Tumors

Radiation therapy has been delivered to dogs either alone, or following an incomplete surgical removal of the tumor. Meningiomas and hypophyseal macroadenomas appear to be the most radioresponsive; however, responses have been seen in dogs with other types of malignant disease.

Thyroid Tumors

Radiation therapy using ¹³¹I has been used to treat thyroid tumors in dogs even when they are not actively secreting hormone. External beam radiation has also been used to treat dogs with unresectable thyroid carcinomas, and 72% of dogs were free of disease three years after treatment. In a compilation of 3 studies, metastases occurred in 14 of 46 dogs (30%) indicating a need for adjunctive chemotherapy in addition to radiation therapy.

Palliative Therapy

Radiation therapy can be given to alleviate the pain and discomfort of a wide variety of malignancies, especially those that involve bone such as osteosarcoma. The risk of late effects is acceptable in terminal patients where the chance of a cure, or even long-term tumor control, is considered remote, and improvement in quality of life for a short period outweighs the higher risks of late effects and tumor recurrence. Despite

the risks of late effects, a German study using RT to a total dose of 32-48 Gray (Gy) delivered once a week in 8 Gy fractions found that there were no significant acute side effects. Late side effects did

not occur within the follow-up period and 88% of the owners were satisfied with this kind of treatment and would choose it again.