Although the diagnosis of cancer is relatively uncommon in horses, tumors do occur in this species. Surgery, radiation, and chemotherapy are traditional cancer treatments in all species. In equine patients, surgery has often been the only treatment offered; however, not all tumors can be controlled with surgery alone. In small animal oncology, newer and better therapies are in demand and available. Radiation therapy is often used to control or palliate tumors locally, especially to satisfy clients who demand sophisticated treatments. The large size of equine patients can make radiation therapy difficult, but it is a valuable tool for treating cancer and should not be overlooked when treating horses.

**How Radiation Therapy Works**

Radiation therapy works primarily by deposition of energy on or near cell DNA. DNA can be damaged directly by radiation or indirectly via formation of oxygen free radicals. Cells with damaged DNA die when they try to divide. Because radiation does not selectively affect cancer cells—it primarily targets any rapidly growing tissue—normal cells and cancer cells are damaged by exposure to radiation. Normal tissue can be spared during radiation therapy by modifying how (i.e., time from beginning to end of radiation, total dose, and dose fractionation) and where (i.e., treatment planning to exclude normal tissue) the dose is delivered. If a single, rapidly delivered, large dose of radiation is administered, it may kill the tumor but also severely damage normal tissue. Survival of normal tissue can be improved when radiation is administered over a prolonged time or fractionated into many small doses.

Factors affecting cellular sensitivity to radiation therapy are ability to repair, ability to repopulate, cell cycle stage, and presence of oxygen. These factors are often called the four Rs: repair, repopulation, redistribution, and reoxygenation. Cells have varying abilities to individually repair sublethal damage induced by radiation. Cells that remain viable after radiation can also repopulate, compensating for the loss of some cells within the particular tissue. When cells redistribute into different stages of their cell cycle, they may become more sensitive to radiation. Because of the indirect effect of oxygen free radicals, the presence of oxygen is critical to improving cell kill with radiation. Theoretically, the four Rs change over time during slow, constant delivery of radiation or after administration of a fractionated dose of radiation. Some cells are destroyed, some recover (preferably, normal cells), and some become more sensitive to radiation (preferably, tumor cells). The four Rs should be considered when deciding how to best fractionate radiation protocols. The goal is to kill the maximum number of tumor cells but allow time for repair and repopulation of normal cells so they survive. A single, large dose can be used if delivered slowly, which is ultimately like fractionation because it allows repair of sublethal damage during treatment. A single, large fraction can be administered quickly only if the dose is...
selectively delivered to tumor tissue while surrounding tissue is physically spared.

When fractionated radiation is used, a total dose of radiation is chosen based on what is needed to kill the tumor, a time interval is chosen based on the tumor and the normal surrounding tissue, and a fraction size is chosen based on the tissue in the field with the least ability to cope with large doses of radiation (i.e., late-responding tissue or tissue with the most catastrophic effects when repair fails to occur [e.g., nervous tissue, bone, fibrous layers in skin]). A radiation treatment dose is measured as a unit of energy absorbed, which is called a gray (Gy). Typical fractionation schemes in small animals are 2 to 3 Gy/day, Monday through Friday, for a total of 18 to 20 fractions. Tumors deemed incurable due to size (not enough can be removed surgically to make a difference) or metastatic potential (e.g., melanomas) can be treated with more aggressive, more coarsely fractionated protocols (6 to 8 Gy three to five times in a 2- to 3-week period) because the patient is not expected to live long enough to experience the “late” adverse effects of radiation described below.

When a discrete tumor is considered for radiation therapy, other factors become involved. Only a constant proportion of cells is killed with each dose of radiation, particularly when the dose is fractionated. Thus, it is important to use radiation when the number of tumor cells is low. Often, the best plan is to decrease the tumor size and increase the sensitivity of the tumor cells by surgically debulking the tumor: removing the entire tumor or at least all that is visible. Radiation is then expected to clean up microscopic dirty margins. For some tumor types, debulking can be helpful before radiation; for other tumor types, this process can create additional problems. This is why determination of tumor type and extent is critical before surgery. The sensitivity of surrounding tissue to radiation also needs to be considered; this cannot be changed and can limit the dose used to treat the tumor. The goal of radiation treatment planning is to deliver the highest possible dose to the tumor and the lowest possible dose to normal surrounding tissue. This may sound easy to do, but it can be quite difficult and even impossible, particularly in large body parts of equine patients. Generally, doses have to be adapted to spare neurologic tissue and bone (fraction size and total dose), but the need to avoid the eyes, oral cavity, and other sensitive structures can also limit radiation’s ability to cure. Treatment can be planned manually by using graphs that show the penetration level of radiation for a particular source or type of radiation. For deep-seated tumors that require imaging for assessment, computerized treatment plans based on the images are the most accurate for predicting what the treatment will deliver to the tumor and normal tissue.

Despite the best attempts to spare normal tissue, radiation therapy has adverse effects, which can generally be divided into early and late effects. Early effects happen within 3 months after therapy, are expected, and will resolve. Early effects involve cells that are rapidly dividing. They include hair loss, skin irritation due to absence of the cornified outer layer of the skin, mucositis, and conjunctivitis. Symptomatic therapy and patience are generally the best approach for treating early adverse effects, and care must be taken not to damage the tissue further (e.g., scratching by the patient, scrubbing by caretakers). Late effects occur months or years after radiation therapy and do not improve. Acceptable late effects include alopecia, hyperpigmentation of the skin, and cataract formation. Less acceptable effects include nervous tissue atrophy or necrosis, bone necrosis, and skin fibrosis. These serious adverse effects may indicate that the treatment was administered improperly.

**Types of Radiation Used in Equids**

**Brachytherapy**

Brachytherapy (short-distance radiation therapy) involves delivery of radiation very close to or, usually, within the tumor. Interstitial therapy (implanting small seeds of radioactive material in a tumor) is the ideal way to treat many superficial tumors because treatment is confined to the tumor area. Sources generally deliver a low dose rate, but because they are left in place and exposure is constant, a relatively high total dose of radiation is delivered over a short time (i.e., 6 days to 2 weeks, depending on the source and its activity). Implantation can be performed using local anesthesia or during a single general anesthetic episode. Many types of interstitial seeds have been used in equine patients, with the main variable being
the half-life of the radioactive source (TABLE 1).\(^1\)–\(^11\) Implants can be placed temporarily or permanently. With permanently placed seeds, the dose is delivered slowly as the radioactive source decays. Temporary implants are meant to be removed after the desired dose of radiation has been delivered. Seeds are surgically implanted using preplaced nylon catheters into which the radioactive sources are inserted using a long-handled forceps. Because people handling seeds and treating equine patients with implants could be exposed to radiation, some states and facilities no longer allow interstitial therapy in horses. Temporary implants must be removed, which is another potential source of human exposure. An alternative is to use a remote after-loading device with a single high-activity source (iridium 192). With this device, after placement of the catheters, the source enters each catheter by computer control for a prescribed distance and time, allowing treatment of the entire tumor. This form of brachytherapy delivers a high dose rate in a short time, thereby fractionating the treatment.

Interstitial implants have been used effectively to treat cutaneous squamous cell carcinoma (SCC) and sarcoids in equine patients. Important factors in determining the success of therapy include tumor size and total dose of radiation. Small tumors are better controlled; therefore, large tumors are usually surgically debulked before radiation therapy. Early studies (in 1978) using cesium or cobalt for pericellular SCC showed 2-year tumor control rates of 68\%.\(^1\) Subsequent studies with various isotopes have shown 2-year tumor control rates of approximately 70\%. Control at 4 years is the best estimate of cure. Treatment of sarcoids has resulted in slightly higher success rates (87\% to 100\%).\(^1\)–\(^12\)

Although brachytherapy is highly successful, it does have complications and poses a potential hazard to equine patients and humans involved in their care. The dose of radiation is determined by the source’s time of decay, the time that temporary implants are left in place, and the proximity of the implants to each other. With precise planning, the dose can be evenly distributed and hot spots avoided. Equine patients are placed in isolation but still have some human contact. Complications include the following:

### TABLE 1 Radioactive Sources for Interstitial Therapy\(^1\)–\(^11\)

<table>
<thead>
<tr>
<th>Radioactive Source</th>
<th>Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cesium 137</td>
<td>30 years</td>
</tr>
<tr>
<td>Cobalt 60</td>
<td>5.26 years</td>
</tr>
<tr>
<td>Gold 198</td>
<td>2.7 days</td>
</tr>
<tr>
<td>Iodine 125</td>
<td>60.2 days</td>
</tr>
<tr>
<td>Iridium 192</td>
<td>74.2 days</td>
</tr>
<tr>
<td>Radon 222</td>
<td>3.83 days</td>
</tr>
</tbody>
</table>

- Treatment around the eye can result in irradiation of the eye, which cannot be shielded during treatment.
- Equine patients with implanted radioactive seeds may rub the tumor, dislodging the seeds and contaminating the stall.

**Plesiotherapy**

Plesiotherapy (very short-distance radiation therapy) involves treatment with a strontium 90 source. This \(\beta\) ray–emitting source is handheld and can treat an area of approximately 5 to 8 mm in diameter. The maximum penetration of \(\beta\)-ray radiation into tissue is only 3 mm, with 60\% of the dose being delivered within the first 1 mm. Use of strontium 90 for radiation therapy is limited to small, superficial tumors, often for postsurgical treatment.\(^4\)–\(^9\),\(^13\) For a single treatment site, approximately 10 to 15 minutes is needed, and multiple contiguous sites can be treated to encompass a larger area. Generally, equine patients must be placed under general anesthesia or be heavily sedated for this therapy.

**Teletherapy**

Teletherapy (long-distance radiation therapy) involves using external-beam radiation to treat a tumor at any depth. Most external-beam radiation is delivered using a linear accelerator capable of producing two distinct forms of radiation: electrons and photons. Use of electron beams allows precise application of superficial treatments. For photon therapy, accelerated electrons strike a target, generating photon beams much like a diagnostic radiography unit does but with much higher energy (at least 6 MeV). These high-energy beams penetrate more deeply into tissue. High-dose therapy is delivered to a localized field; however,
surrounding tissue is also treated. Therapy is nearly always fractionated to improve tumor kill and reduce adverse effects to surrounding tissue. Because the beam is stationary, the patient must remain absolutely still to ensure that the treatment is administered to the correct area. No staff member should be in the room during the therapy. This therapy requires repeated general anesthesia with its associated risks.

Many longstanding biases against using teletherapy in equine patients exist. The need for repeated general anesthesia is often a major deterrent. Even today, facilities that can irradiate equine patients often use hypofractionated protocols or protocols involving many fewer fractions of therapy than would be used for small animals with the same tumor. Teletherapy facilities must be built with equine treatment in mind. Linear accelerators are costly, and rooms with maximal shielding are required to house them. Small animals can be treated on a treatment couch designed for humans, and they are often anesthetized in the same room. Equine patients need their own treatment tables, and anesthesia is induced at another location, requiring patients to be transported into the treatment room. Everything used with linear accelerators must be modified for equine patients (e.g., anesthesia equipment, monitors). Because of these concerns, bias against using teletherapy to treat equine tumors persists despite good results of all other forms of radiation therapy.

Outcomes were significantly better in horses with SCC of the eyelid and periocular structures that were treated with adjuvant radiation therapy than in horses that were not treated with this therapy, with recurrence rates of 11.9% and 44.1%, respectively.

External-beam radiation has been used on a limited basis to treat deep-seated tumors in horses. Reports of treatment include a mandibular ossifying fibroma that had not returned after 2 years; SCC of the nasal cavity and paranasal sinuses in three horses that survived 2.5, 3.5, and 6 years; and a recurrent paranasal sinus ossifying fibroma in a horse in which a tumor was controlled for longer than 6 years. Unpublished cases are likely numerous but are still much fewer than cases currently reported in small animal oncology. Various equine tumors (e.g., head and extremity SCC, osteoma, fibroma, ameloblastoma of the oral cavity, melanoma, nasal tumor) have been successfully treated with radiation therapy at several institutions (TABLE 2). The adverse effects of radiation are generally minimal. These results have frequently been attained with fairly coarsely fractionated protocols, meaning fewer and larger dose fractions than would be considered ideal for small animals or humans.

At Washington State University (BOX 1), equine patients with cutaneous SCC have been treated twice daily (6 hours apart) for 7 days (treatment was not administered on weekends). Similar radiation protocols have been

<table>
<thead>
<tr>
<th>Location</th>
<th>Types of Radiation</th>
<th>Contact Person</th>
<th>Telephone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auburn University Auburn, Alabama</td>
<td>Teletherapy: linear accelerator Brachytherapy</td>
<td>Dr. Bill Brawner Dr. Greg Almond</td>
<td>334-884-5045</td>
</tr>
<tr>
<td>University of Missouri Columbia, Missouri</td>
<td>Teletherapy: linear accelerator Brachytherapy</td>
<td>Dr. Jimmy Lattimer</td>
<td>573-882-7821</td>
</tr>
<tr>
<td>The Ohio State University Columbus, Ohio</td>
<td>Teletherapy: linear accelerator</td>
<td>Dr. Eric Green</td>
<td>614-292-6661</td>
</tr>
<tr>
<td>Texas A&amp;M University College Station, Texas</td>
<td>Teletherapy: linear accelerator Brachytherapy</td>
<td>Dr. Michael Walker</td>
<td>979-845-9081</td>
</tr>
<tr>
<td>University of California, Davis</td>
<td>Teletherapy: linear accelerator Brachytherapy</td>
<td>Dr. Alain Theon</td>
<td>530-752-2517</td>
</tr>
<tr>
<td>Washington State University Pullman, Washington</td>
<td>Teletherapy: linear accelerator</td>
<td>Dr. Janean Fidel</td>
<td>509-335-0711</td>
</tr>
</tbody>
</table>
used to treat feline and human SCC, with the best results in patients with rapidly growing tumors that have little recovery time between treatments. The short treatment time closely approximates the treatment time associated with interstitial radiation. This protocol is not ideal for every tumor or location but may be useful in certain cases.

CONCLUSION

Many equine tumors should be considered for radiation therapy. One of the few treatment criteria is that the tumor has not metastasized and has no tendency to metastasize. Location can make treatment easier; the extremities and head are much easier to position, but other areas of the body can be treated if they fit under the beam. Melanomas and sarcoïds can be treated quite effectively with large-fraction radiation (only three or four doses of 6 to 8 Gy). SCCs respond well to various protocols, and radiation should be considered the ideal therapy for nonresectable SCCs. Lymphosarcoma in a single location responds rapidly to radiation therapy. The cost of radiation therapy can be a deterrent, but if owners can be offered a treatment that will give their horse an additional 2 to 10 years of life without loss of a body part such as an eye, they may be willing to spend $2000 to $6000. Travel to treatment facilities can be a problem, but facilities can be found throughout the United States. Perhaps radiation therapy will be used more often in equine patients as more practitioners become familiar with its uses and benefits.
References