For Richard and Monica Smith, it started simply as a small area of hair loss on their eight-year-old Shetland Sheepdog, Corky's, left tarsus. Two days later, the spot had grown into a small mass and by the end of the week, it was the size of a golf ball. Understandably concerned, the Smiths consulted their veterinarian and had the mass removed. The histopathology report described the mass as a low-grade (grade 1) hemangiopericytoma. The tumor was incompletely removed, a common problem with masses on the extremities where insufficient tissue is present for complete surgical resections.

Corky was referred to the OSU Medical Oncology service to stage his disease and pursue additional treatment options. Thoracic radiographs and fine needle aspirates of his left popliteal lymph node showed that the tumor had not spread to these locations. Now the focus of treatment was addressing the microscopic disease that remained at the surgical site. Potential treatment options considered included local infiltration with chemotherapy, radiation therapy and amputation.

Hemangiopericytomas, or peripheral nerve sheath tumors, are generally slow growing tumors with variable rates of metastasis, with the risk of metastasis being largely dependent on the histologic grade. Because Corky’s tumor was a grade 1, there was only about a 10% risk of metastatic spread. The Smiths chose to pursue radiation therapy.

In Corky’s case, his radiation protocol consisted of 19 treatments of daily radiation, each delivered under general anesthesia. With this regimen, it is expected that greater than 80 to 90% of patients will not have recurrence within 3 to 5 years. Because of Corky's close attachment to his sister Kaylee, the Smiths decided to have both Corky and Kaylee stay at OSU during Corky's therapy.

As expected with this protocol, Corky did develop side effects, moist desquamation of the skin, in the treatment area, a region three centimeters around his scar. The moist desquamation began during the last week of treatment and lasted for about three weeks. The affected area was treated with antibiotics, pain medications, and an E-collar to keep him from licking the site.

Today, nearly 21 months after his treatment, Corky is feeling great. He visits his veterinarian regularly for routine reevaluation of the radiation site and has no evidence of tumor regrowth.

Additional tumors for which radiation therapy may play a beneficial role in treatment:
Soft Tissue Sarcomas, Brain Tumors, Oral tumors (Squamous Cell Carcinoma, Melanoma, Fibrosarcoma), Mast Cell Tumors, Osteosarcoma, and Nasal Tumors
The Oncology/Hematology Service recently began a new clinical trial, investigating the pharmacokinetics of high-dose intermittent oral artemisinin in dogs with spontaneous tumors. Dr. Kenji Hosoya, resident in Radiation Oncology, investigated the effects of artemisinin on cancer cells in culture. Due to his laboratory findings, we are now investigating the use of artemisinin for the treatment of tumors in dogs.

What is artemisinin? Artemisinin is an extract from the plant *Artemisia annua* L., which is used in traditional Chinese medicine (TCM). It was first identified and isolated in 1972 in a project to discover new antimalarial drugs from TCM launched by the Chinese government and now is the first-line treatment for malaria in South Asia.

Artemisinin also has been shown to have toxic effects in several types of human cancer cells *in vitro*. Dr. Hosoya has demonstrated a similar ability for artemisinin to induce cell death in several types of canine cancer cells *in vitro*. Artemisinin has been used to a limited extent for clinical cancer treatment in people and anecdotally in dogs with osteosarcoma, with daily administration of small doses. However, there are few reports of successful outcomes.

Studies of continuous oral artemisinin administration revealed a remarkable time-dependent decrease in bioavailability that occurs within 7 days. The currently used dose of artemisinin for cancer patients seems inappropriately low compared to the potentially needed target plasma concentration, based on *in vitro* data collected by Dr. Hosoya.

The current on-going clinical trial will investigate if the absorption resistance can be avoided by pulse-dosing artemisinin and will also evaluate the therapeutic effects of artemisinin in tumor-bearing dogs.

**Clinical Trials**

**On-Going Clinical Trials**

- Gene expression profiling of canine lymphoma
- Oral artemisinin in dogs with spontaneous tumors
- Copy number polymorphisms in dogs
- DNA methylation in canine lymphoma
- Rapid release paclitaxel particles for intravesical treatment of transitional cell carcinoma

**Upcoming Clinical Trials**

- Evaluation of Rapamycin (a mTOR inhibitor) in dogs with osteosarcoma
Radiation therapy is the use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine or from materials placed in the body. At The Ohio State University, a linear accelerator is used to deliver radiation treatments. This is the equipment most commonly used in human medicine. It delivers a uniform dose of high-energy x-rays to the targeted area of the patient. The radiation can be delivered to the patient’s tumor from any angle in an attempt to avoid excessively irradiating normal tissue. The radiation kills tumors cells and shrinks tumors that may not be affected by chemotherapy or safely removable by surgery. It does this by damaging the DNA of the tumor, causing the tumor cells to die. Radiation therapy often is used in conjunction with chemotherapy and/or surgery.

Radiation treatments are either definitive or palliative in their intent. Definitive therapy is given in a course of treatments that can last 2-4 weeks, depending on the tumor type. This schedule delivers a large total radiation dose to the tumor in many small fractions, each given once a day. This helps to protect normal healthy tissue from being excessively damaged. Palliative therapy is designed to relieve cancer related discomfort or pain in the patient with disease when the likelihood for definitive control is low. Treatment is typically given once a week for four weeks and rarely causes any side effects.

Radiation therapy in dogs and cats typically does not cause any systemic side effects such as nausea or decreased appetite. Some patients may experience fatigue due to repeated anesthesia. Direct side effects of the radiation at the treatment site are more common. Acute side effects are those effects that occur shortly after the treatment is over and can be expected with definitive protocols. They occur in tissues within the treatment field and are due to the death of rapidly dividing normal cells like skin and mucous membranes. These side effects are generally managed conservatively with antibiotics and pain medications and heal on their own within 2 to 3 weeks. Late effects are those that occur well after the conclusion of radiation therapy and are usually related to death of the endothelial cells (those cells lining blood vessels). This results in side effects that are specific to the tissues in the treatment field (osteoradionecrosis, fibrosis, demyelination, etc...). Late effects are more likely to occur when palliative protocols are used, so these protocols are reserved for patients where long-term survival is not likely.

Article written by Dr. Eric Green.

Right: Computer generated image used for mapping targeted area for treatment.
Above: Patient undergoing treatment in the linear accelerator.
Signalment:
A female, 7-year-old Pitbull Terrier presented to the Surgery Service for evaluation of an ulcerated mass of the pinna of her left ear. The mass was removed and sent for histopathology.

What is your diagnosis?

Above: Representative cytology from a fine needle aspirate (FNA) of the tumor. Wright’s-Giemsa, 100X
Below: Histopathology of the ear mass. H&E, 10 X
Left: Histopathology of the ear mass. H&E, 40 X

What is your cytologic and histologic description?
What is your diagnosis?
The answers are on the next page.
**Diagnosis: Hemangiopericytoma**

**Cytologic description:** Large aggregates of spindle to stellate shaped cells. Moderate to abundant, lightly basophilic cytoplasm with indiscreet cytoplasmic borders or veiling appearance. The nuclei are round to oval with a coarse chromatin pattern. One to many small prominent nucleoli.

**Histopathologic description:** Poorly demarcated sheets of moderately pleomorphic spindle cells that occasionally form perivascular whorls.

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**Review of Hemangiopericytomas**

Hemangiopericytomas are common malignant tumor of subcutaneous origin in dogs. This tumor is a member of the soft tissue sarcoma family, adjuvant radiation therapy, or infiltrating the site. This family of tumors is a diverse group of tumors, with local chemotherapy. Long term control is which comprise about 15% of all skin and usually achievable with Grade 1 and 2 subcutaneous tumors. They are most often found hemangiopericytomas.

These tumors have a low incidence of metastasis but the rate is dependent on histologic grade. They are known to be locally aggressive and often locally recur. As with all soft tissue sarcomas, staging prior to treatment is important. This should consist of three view thoracic radiographs and regional lymph node assessment with either FNA or biopsy.

Histology is important for assessing risk for metastasis and evaluating surgical margins. Grades 1 or 2 tumors have a 10% to 20% rate of metastasis. Grade 3 tumors have a much higher metastatic rate, but are relatively uncommon.

For information on the Clinical Trials please contact, Jill Yaissle, DVM, MS (yaissle.1@osu.edu) or for information concerning the Greyhound Program please contact, Liliana Marin, DVM (marin.25@osu.edu) at (614) 292-0950.

Appointments for Medical Oncology are scheduled by calling OSU-VTH at (614) 292-3551, please ask for any other following individuals:

Stacey Gallant, RVT; Nicole Westendorf, RVT; Janet Charske, RVT

Appointments for Radiation Oncology are scheduled by calling OSU-VTH at (614) 292-3551. Please ask for Eric Green, DVM, DACR (Radiology and Radiation Oncology).

**WEBSITES:**

Oncology/Hematology: vet.osu.edu/564.htm  Blood bank: vet.osu.edu/bloodbank.htm

Chemotherapy Protocols: vet.osu.edu/1359.htm  Greyhound Information: vet.osu.edu/1872.htm

You can be part of improving animals' lives through your generous donation. For information about giving to these and other programs please contact Karen Longbrake, Director of Development at (614) 688-8433 or Longbrake.1@osu.edu.