

## **Evaluation of Efficacy of Palliative Radiation Protocols Using Force Plate Analysis in Dogs with Appendicular Osteosarcoma**

Principle Investigator: Sarah Boston, DVM, DVSc, Diplomate ACVS  
DVSc Student: Michelle Oblak, Small Animal Surgery Resident

Thank you for your interest in participating in our Pet Trust funded study to evaluate the efficacy of palliative radiation therapy in the treatment of canine appendicular osteosarcoma. We hope that this information sheet will provide you with the information you need to discuss possible referral of a case to the Ontario Veterinary College. If you have a potential case to refer for this study, or if you have any questions regarding this study, please do not hesitate to contact us.

### **Outline:**

- Eligible patients are dogs with an osteosarcoma of the limb with no evidence of pulmonary metastasis
- The patients will be treated with one of two palliative radiation therapy protocols
- The addition of chemotherapy protocols will be discussed with the owners and will be optional
- Patients will be evaluated regularly at OVC using force plate analysis to assess limb use
- If the owners complete the study, the cost of palliative radiation will be covered
- The cost of chemotherapy, if elected, will be paid by the owner

### **Introduction**

Palliative radiation is a common method for the palliation of bone cancer pain in human and animal cancer patients. It is an effective method for treating bone cancer pain. The exact mechanism of pain relief is not known. However, it is probably a combination of a decrease in osteoclast activity, a decrease in tumor burden and a decrease in inflammatory cells. As in people, canine patients have a high reported response to palliative radiation (74-96%). Duration of pain relief in dogs varies from 1.8-4.3 months. The optimal protocol for palliative radiation in dogs is not known. Most published protocols for canine osteosarcoma use an 8Gy dose given at weekly intervals for 2-4 treatments. The most common protocol is given at days 0, 7 and 21 days. However, at CSU and WCVM, the protocol is 8Gy given on day 0 and 1. A third or fourth dose is administered when the patient relapses. To date, there are no studies in canine patients to indicate which protocol is superior. In human patients, a recent study showed no difference in efficacy between single large doses of radiation versus more fractionated protocols. A further problem in our patients is that the response rate is generally measured by the owner. Further, duration of effect and/or survival times are based on when the owner elects to stop treatment. Although this will be a reflection of the patient's pain control, it is not an objective measure of pain relief and the placebo effect of radiation, coupled with the owners desire not to euthanize their pet, may falsely increase reported

response rates and survival times. These responses could therefore be an inaccurate reflection of our ability to control pain in our patients with radiation. Objective measures are necessary to determine both the efficacy of palliative radiation in general and the optimal protocol.

The addition of chemotherapy to palliative radiation protocols is controversial, with some studies reporting an increase in the response rate and duration of effect with chemotherapy and other studies reporting no effect. Direct killing of tumor cells by the chemotherapeutic agent has been reported to have an analgesic effect in people when preoperative neoadjuvant chemotherapy is administered for osteosarcoma. Systemic chemotherapy will be useful in cases of palliative radiation to suppress metastatic disease. This will be helpful in cases that have had a positive and durable response to local therapy.

An optimal palliative approach to bone cancer in dogs would treat the bone cancer pain by multiple modalities, while still aiming to suppress metastatic disease. Additional treatment with pamidronate will reduce bone osteolysis to decrease pain. Chemotherapy can also be added to this regimen to treat the primary tumor as well as metastases. Ongoing treatment with NSAIDs and gabapentin should help to control ongoing pain associated with bone cancer.

Subjective methods of evaluating the effect of these modalities include assessment of response by both the owner and the attending clinicians. The visual analogue scale (VAS) has been shown to be a reliable method for subjective evaluation of limb use in canine patients. More objective measures of response would include force plate analysis and a measure of patient activity. Evaluation of the ground reaction forces is a direct measure of the amount of force that the patient will place through the limb and, therefore is a measure of the amount of pain induced by limb use. This method of limb use evaluation has been reported in the veterinary literature primarily for the study of osteoarthritis. However, this is a very well-established technique for evaluating the degree of lameness and limb pain in canine patients. This method has not been previously reported in the literature to evaluate the efficacy of palliative radiation, but was reported at the most recent VCS as a method to compare dogs receiving palliative radiation with and without pamidronate.

### **Objectives**

1. The objective evaluation of palliative radiation as a tool for pain management in canine patients with appendicular osteosarcoma using force plate analysis
2. The subjective evaluation of palliative radiation as a tool for pain management in canine patients with appendicular osteosarcoma via clinician evaluation and client questionnaires.
3. The objective comparison of two palliative radiation protocols for efficacy in canine appendicular osteosarcoma patients.
4. The objective and subjective comparison of patients treated with palliative radiation and analgesics alone versus palliative radiation, analgesics, pamidronate and chemotherapy.

## **Hypotheses**

1. Palliative radiation is an effective treatment method for bone cancer pain in dogs.
2. A 0, 7, 21 protocol will have a similar efficacy to a 0,1 protocol for bone cancer pain in dogs.
3. Dogs treated with palliative radiation and analgesics will have a shorter duration of efficacy compared with dogs treated with palliative radiation, analgesics, pamidronate and chemotherapy.

## **Materials and Methods**

Study Criteria:

1. Canine appendicular osteosarcoma (histologic or presumptive radiographic diagnosis)
2. Negative for gross metastatic disease on thoracic radiographs +/- long bone survey radiographs/ bone scan
3. Weight bearing on the affect limb
4. Owner consent

Twenty dogs will be evaluated. Dogs will be randomly assigned to one of two treatment groups. Group one will receive 8Gy of radiation to the site on days 0 and 1. Group two will receive 8Gy of radiation to the limb on days 0,7 and 21. Prior to receiving the first radiation dose, dogs will be assessed for limb use with force plate analysis. Dogs who are on NSAIDs at the time of study enrollment will stay on this medication for the duration of the study unless contraindicated. Dogs who are not on an NSAID will be prescribed Meloxicam for 5 days prior to baseline force plate analysis. Adjunctive therapy will be discussed with the clients. Standard chemotherapy and pamidronate will be offered to the clients and the decision to pursue this adjunctive treatment will be client-driven.

The owners will be asked to complete a VAS questionnaire weekly regarding limb use and quality of life. At each visit, the questionnaire will also be completed by the attending clinician. If the patient appears to be clinically worse but continues to use the limb and is assessed to have a good quality of life by both the attending clinician and owner, gabapentin and tramadol will be added to the analgesic protocol.

End-points for the study will include: a perception of a poor quality of life by either the owner or attending clinician, death or euthanasia, pathologic fracture or if the patient is non-weight bearing on the limb. If the patient is weight bearing but is to be released from the study, a final force plate analysis will be performed prior to removal when feasible.

## **Anticipated Results**

Force plate analysis will be an effective objective tool to measure efficacy of palliative radiation for the treatment of appendicular osteosarcoma. The protocols evaluated will likely have a similar efficacy for the treatment of bone cancer pain. Chemotherapy and pamidronate will likely improve the response rate and duration of response to treatment.

### **Pitfalls and Significance**

Force plate analysis has not been previously used to assess the efficacy of palliative radiation. The optimal palliative radiation protocol is currently unknown. If the day 0, 1 is shown to be as effective as the 0, 7, 21 protocol, this would be a more convenient and less expensive option for owners. As well, palliative radiation outcome studies have historically relied upon owner's feedback. Although this is an important measure, it is not objective and, for this reason, efficacy of this treatment is very difficult to determine. Using force plate analysis to evaluate dogs with osteosarcoma may serve as a model in the future for the assessment of other novel therapies.

A potential pitfall of this study is that the administration of chemotherapy/pamidronate is not randomized. Because of the expense and potential side effects involved with this treatment, the owner must be involved in this decision making process and this cannot therefore be randomized in this clinical trial.

### **How to refer a case for the study**

As for any referral to the OVC, if you have a dog that you suspect has osteosarcoma, an appointment should be scheduled with the Small Animal Medicine or Oncology Services by contacting the Appointment Scheduler at (519)823-8830. All appointments must be made on a referral basis. Once the case has been assessed by a clinician at the OVC the treatment options for osteosarcoma will be discussed with the client. If the client wishes to pursue palliative radiation, they will meet with one of the study investigators to further discuss this study.

### **Financial benefit to the client**

To participate in the study, clients will be responsible for the cost of a consultation, and initial staging involving radiographs of the limb and 3 view thoracic radiographs. We would also recommend further staging including long bone radiographs or a bone scan when available but this is not required to qualify for the study. The cost of radiation therapy will be covered by the study, only if the dog is present for a minimum of 8 forceplate evaluations. If the client chooses to leave the study before this point, the study will be unable to cover the cost of the radiation treatment and they will be billed for the radiation therapy by the hospital at a cost of \$800-1000.

Thank you for your interest in this study. This is meant to be a brief overview of the study. If you would like to review the full Pet Trust proposal or for more information, please do not hesitate to contact me at (519)823-8830 or [moblak@uoguelph.ca](mailto:moblak@uoguelph.ca).

Sincerely,

Michelle Oblak, DVM  
Small Animal Surgery Resident  
Doctor of Veterinary Science (DVSc) Student

Sarah Boston, DVM, DVSc, Diplomate ACVS  
Assistant Professor of Small Animal Surgery  
Soft Tissue and Surgical Oncology