



## Radiation therapy in the treatment of canine lymphoma

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Lymphoma is one of the most frequently diagnosed cancers in dogs (1). Approximately 80% of dogs diagnosed with lymphoma have the multicentric form, which is an anatomic classification based on generalized lymph node involvement (2,3). Current chemotherapy protocols using combinations of drugs provide median survival times of 9 to 12 mo; it has been proposed that the addition of radiation therapy to chemotherapy may increase the remission and survival times (4,5). In the past, the role of radiation therapy in treating canine lymphoma has been primarily for the control of local disease. Radiation therapy has been used effectively in the treatment of solitary lymphoma of bone, nasal cavity, brain, spinal cord, and skin (6–9). Since most dogs with lymphoma on presentation have generalized lymph node or organ involvement (World Health Organization Stage III–IV), irradiation of their whole body would be needed to effectively treat all the cancer cells (2). A single dose of 8 Gy (1 Gy = 100 rad) has been shown to kill more than 99% of lymphocytes *in vitro* (10). However, the dose of radiation that can be administered safely to the whole body of dogs at one time is too low to effectively reduce tumor cell burden (11,12). To allow a higher dose to be administered safely, radiation of one half of the body, followed by the other half 4 wk later, has been proposed (5). Two recent studies have assessed the safety and efficacy of combining 2 sequential half-body radiation treatments with chemotherapy in the treatment of multicentric lymphoma in dogs.

A prospective pilot study at Colorado State University assessed toxicity associated with sequential half-body radiotherapy and chemotherapy for 6 dogs with previously untreated lymphoma (13). A CHOP-based (C from cyclophosphamide, H from hydroxydaunorubicin = doxorubicin, O from Oncovin [Eli Lilly, Indianapolis, Indiana, USA] = vincristine, P from prednisone) chemotherapy protocol was used with cranial half-body irradiation at week 11 and caudal half-body irradiation at week 15 (Table 1) (this CHOP-based protocol uses a combination of l-asparaginase, vincristine, prednisone, doxorubicin, and cyclophosphamide for 25 wk, with no

**Table 1. Dosing schedule for half-body irradiation interposed within a maintenance-free, combination chemotherapy protocol (13)**

Week	Treatment	Dose
1	Vincristine	0.7 mg/m <sup>2</sup> IV
	Asparaginase	10 000 IU/m <sup>2</sup> IM
	Prednisone	2 mg/kg BW PO every 24 h
2	Cyclophosphamide	250 mg/m <sup>2</sup> PO or IV
	Prednisone	1.5 mg/kg BW PO every 24 h
3	Vincristine	0.7 mg/m <sup>2</sup> IV
	Prednisone	1 mg/kg BW PO every 24 h
4	Doxorubicin <sup>a</sup>	30 mg/m <sup>2</sup> IV
	Prednisone	0.5 mg/kg BW PO every 24 h
6	Vincristine	0.7 mg/m <sup>2</sup> IV
	Cyclophosphamide	250 mg/m <sup>2</sup> PO or IV
8	Vincristine	0.7 mg/m <sup>2</sup> IV
	Doxorubicin <sup>a</sup>	30 mg/m <sup>2</sup> IV
11	RT Cranial Half Body	4 Gy × 2 fractions
	Vincristine	0.7 mg/m <sup>2</sup> IV
15	RT Caudal Half Body	4 Gy × 2 fractions
	Cyclophosphamide	250 mg/m <sup>2</sup> PO or IV
19	Vincristine	0.7 mg/m <sup>2</sup> IV
	Doxorubicin <sup>a</sup>	30 mg/m <sup>2</sup> IV
23	Vincristine	0.7 mg/m <sup>2</sup> IV
	Cyclophosphamide	250 mg/m <sup>2</sup> PO or IV
27	Vincristine	0.7 mg/m <sup>2</sup> IV
	Doxorubicin <sup>a</sup>	30 mg/m <sup>2</sup> IV

IV — intravenously; 1 Gy = 100 rad; IM — intramuscularly; h — hour; PO — per os; mg/m<sup>2</sup> — milligram per square meter

<sup>a</sup>Doxorubicin dose is decreased to 1 mg/kg for dogs < 10 kg body weight

maintenance chemotherapy [14]). At week 11, the cranial half of the body was treated with 2 doses of 4 Gy, separated by 24 h. The same protocol was repeated at week 15 for the caudal half of the body. Toxicities associated with radiation include lethargy, hair loss in the treated areas, soft stool, and decreases in neutrophil counts. Overall, the authors found that the protocol was well tolerated. The median remission time in the 6 dogs was 15.2 mo and the median survival was 18.7 mo, supporting further studies of combining radiation therapy with conventional drug therapy for multicentric lymphoma.

Fifty-two dogs with lymphoma received half-body irradiation with induction chemotherapy at North Carolina State University (15). A combination of l-asparaginase, vincristine, prednisone, doxorubicin, and cyclophosphamide was used in this protocol for an 11-week period. Two doses of cranial half-body irradiation 24 h apart were given to dogs in complete remission at week 13, and repeated at week 16 for the caudal half-body. Seventy-five percent of the dogs treated with radiation therapy had Stage IV or V lymphoma. The median overall remission (1st and 2nd remission

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**Figure 1.** Patient setup for caudal half-body irradiation.

duration) was 16.2 mo. The authors compared their results with those of a previous study in which dogs treated with a similar chemotherapy protocol, but without radiation, had a median overall remission of 11 mo (16). This combination chemotherapy and radiation protocol was well tolerated, and the results suggested a lengthened period of remission of canine lymphoma by using half-body radiation therapy after induction chemotherapy compared with the period of remission obtained by using chemotherapy alone.

The half-body radiation protocol used at the Western College of Veterinary Medicine is as described for the pilot study from Colorado State University (13). Dogs are treated on an outpatient basis. Two doses of 4 Gy are given to the cranial half (week 11) and the caudal half (week 15) of the body, 24 h apart. Anesthetized patients are placed in lateral recumbency (Figure 1). Their legs and head are tucked against the body to make the patient as square in shape as possible. The level of the xiphoid process of the sternum is used to define cranial and caudal half-body. Wet towels are placed around the patient to act as tissue equivalent material and to improve radiation dose distribution. Right and left lateral beams are used to deliver the radiation (parallel opposed ports). A postirradiation complete blood cell count is recommended at 10 to 14 d after treatment, prior to the dog receiving the next dose of chemotherapeutic drug.

In the 2 published protocols described above, radiation therapy in combination with chemotherapy, appeared to be well tolerated and, in dogs with multicentric lymphoma, may significantly extend median remission over treatment with chemotherapy alone. Future clinical trials are needed to determine the optimal timing of radiation therapy in relation to chemotherapy.

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