Use of samarium Sm 153 lexidronam for the treatment of dogs with primary tumors of the skull: 20 cases (1986–2006)

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Objective—To evaluate samarium Sm 153 lexidronam (153Sm-EDTMP) as a treatment option for dogs with bony tumors of the skull.

Design—Retrospective case series.

Animals—Dogs with multilobular osteochondrosarcoma (MLO) or osteosarcoma (OSA) of the skull.

Procedures—Veterinary Medical Teaching Hospital records from the Universities of Missouri and Florida from 1986 to 2006 were searched for dogs with primary skull tumors treated with 153Sm-EDTMP.

Results—25 dogs were initially evaluated, with 5 dogs subsequently excluded because of inadequate follow-up or unrelated death. Seven OSAs and 13 MLOs were diagnosed. Tumors involved the occipital and frontal bones (n = 10), zygomatic arch and maxilla region (6), palate (3), and mandible (1). No clinically important adverse effects related to 153Sm-EDTMP treatment were documented. Of the 20 dogs evaluated 21 days after injection with 153Sm-EDTMP, 4 had subjective improvement, 13 had progressive disease, and 3 had insufficient follow-up. On the basis of radiographic findings, metastasis was suspected in 1 dog; 16 dogs had no metastasis evident, and medical records were insufficient for 3 dogs. Survival time, defined as the 153Sm-EDTMP injection date to the date of death, ranged from 3 to 1,314 days (median, 144 days).

Conclusions and Clinical Relevance—The subjective improvement in 4 patients and lack of clinical evidence of adverse effects suggested that 153Sm-EDTMP injection may be an option for the treatment of dogs with MLO or OSA of the skull when other treatments have failed or surgery is not possible. (J Am Vet Med Assoc 2012;240:1310–1315)

Samarium Sm 153 lexidronam is a radiopharmaceutical with demonstrated antitumor properties and efficacy for pain palliation in the treatment of skeletal neoplasia. Palliative and even curative effects have previously been demonstrated in dogs receiving 153Sm-EDTMP for the treatment of skeletal neoplasia, including primary tumors and secondary metastatic disease. Although limited, these previous clinical studies1,2 provide support for 153Sm-EDTMP as a therapeutic option for patients with primary bone tumors that are not candidates for other established treatments. In veterinary medicine, 153Sm-EDTMP has primarily been used in the treatment of appendicular tumors; however, the bone-targeting radiopharmaceutical presents an attractive alternative treatment for patients with inoperable bony tumors of the skull. A previous study3 of dogs examining the clinical response of bone tumors treated with 153Sm-EDTMP indicated a good response rate (response determined by functional improvement and radiographic involution of the lesion) in patients with tumors of the axial skeleton, heavily calcified or ossified lesions, tumors that had not broken through the cortex of the bone, and small metastatic lesions (diameter, < 2.0 cm). In the authors’ clinical experience, many primary bony tumors of the skull, such as purely osteoprodutive OAs of the calvarium, possess ≥ 1 of these tumor characteristics.

Various tumor types have been reported to affect the skull in dogs; the 2 most common primary bony tumors of the skull are MLO and OSA. Osteosarcoma

ABBREVIATIONS

153Sm-EDTMP  Samarium Sm 153 lexidronam
MLO   Multilobular osteochondrosarcoma
MST   Median survival time
OSA   Osteosarcoma
Osteosarcoma originating from the axial skeleton accounts for approximately 25% of all OSAs diagnosed in dogs. 3–8 It has been our clinical experience that OSA of the calvarium has a tendency to be purely osteoprodutive, a feature of this tumor which was reported some years ago. 10 Multilobular osteochondrosarcoma is a tumor composed of bone or partially to completely calcified tissue and is surrounded by mesenchymal tissue or stroma. 11 Multilobular osteochondrosarcomas are slow growing, locally invasive, compressive tumors with a low overall metastatic rate. 11–16

The purpose of study reported here was to evaluate 153Sm-EDTMP as a treatment for dogs with primary bony tumors of the skull, when surgical excision was not an option because of tumor location and in which the use of nuclear scintigraphy with 99mTc-methylene diphosphonate tumor uptake suggested potential efficacy of this treatment.

Materials and Methods

Medical records from the University of Missouri Veterinary Medical Teaching Hospital and the University of Florida Veterinary Medical Teaching Hospital from September 1986 through July 2006 were searched for dogs fulfilling the selection criteria to be included in this retrospective study. The selection criteria were limited to dogs with a histologically confirmed primary malignant bone tumor of the skull receiving administration of 153Sm-EDTMP at the target dose of 1.0 mCi/kg (0.45 mCi/lb; 37 MBq/kg [16.8 MBq/lb]). All dogs received 153Sm-EDTMP as a primary treatment or as an adjunct to previous treatment. During 153Sm-EDTMP treatment, patients were not given any concurrent anti-neoplastic treatments.

The following parameters were evaluated in all eligible patients: tumor type, tumor location, age at time of treatment, breed, sex, weight, dates of diagnosis and 153Sm-EDTMP injection, date of death, survival time from 153Sm-EDTMP injection until death, subjective improvement 21 days after injection, other treatments prior to 153Sm-EDTMP injection, and the presence of metastasis, ocular involvement, and any preexisting clinical signs or concurrent illness. All primary bone tumors involving the flat bones of the skull, mandible, maxilla, and hard palate were included. Tumor type was classified on the basis of results of histologic examination. Tumor location was further defined as occipital and frontal bones, zygomatic arch and maxilla, palate, or mandible. Signalment was classified into categories on the basis of sex (sexually intact male, castrated male, sexually intact female, and spayed female), age (< 7 years or ≥ 7 years), breed (purebred or mixed), and weight (< 25 kg [55 lb] or ≥ 25 kg). To divide groups with adequate numbers to perform analysis, 7 years of age and 25 kg were selected as the desired cutoff points. Patients were not excluded on the basis of the presence or absence of metastasis, preexisting clinical signs, concurrent illness, previous treatments, or signalment.

Patient records and direct communication with the referring veterinarians or clients were used to evaluate the following variables: date of diagnosis, date of 153Sm-EDTMP injection, date of death, previous treatments, presence of metastatic disease, ocular involvement, preexisting clinical signs, or concurrent illnesses. The measurement of hematologic and clinical chemistry variables prior to and after treatment was not consistent or able to be documented in all cases and was not included in the retrospective evaluation. As used in a prior retrospective study of 35 dogs with primary bone tumors treated with 153Sm-EDTMP, tumor response was evaluated on the basis of subjective improvement. Subjective evaluation 21 days after 153Sm-EDTMP injection was on the basis of clinician or owner perception. Clinicians and owners were asked to classify patients into 1 of 4 categories: complete resolution of disease; improved with a visible reduction in tumor size, associated clinical improvement, or both; stable disease with no visible progression or reduction in tumor size or patient status; and progressive disease with prolonged or continued enlargement of the tumor, worsening of clinical status, or both. Date of 153Sm-EDTMP injection in relation to date of death was used to determine the overall survival time. The date of injection and the recorded date of death were used to determine a correlation between the time periods from diagnosis to treatment, in relation to the overall MST. Dogs were grouped into 3 categories according to the duration between diagnosis and treatment: within 1 to 25 days, 26 to 50 days, or ≥ 51 days following diagnosis. These time periods were selected on the basis of a natural break among the population evaluated. All 3 time periods were analyzed as a group by use of the Kaplan-Meier proportional hazards method.

Variables, including age group, sex, location of the tumor, tumor type, previous treatments, preexisting clinical signs or concurrent illness, and number of days from diagnosis to 153Sm-EDTMP treatment, were individually analyzed by use of the Kaplan-Meier proportional hazards method. Because of the descriptive nature of this retrospective study, the variables were analyzed with a univariate approach. Survival time was defined from the day of 153Sm-EDTMP treatment to the date of death because of tumor or treatment. Alternative outcomes including being alive at the time of data analysis and being lost to follow-up were censored in the survival analysis. Patients with minimal follow-up information and inadequate overall usable data or a documented death because of an unrelated cause were excluded from the study. A value of $P < 0.05$ was considered significant.

Results

Twenty-five dogs with OSA or MLO involving the flat bones of the skull, hard palate, mandibular, or maxillary bones fulfilled all initial requirements for study inclusion. Of these 25 dogs, 4 were excluded from the study because of inadequate follow-up information and 1 dog was excluded because of inadequate usable data as well as a documented unrelated death caused by a house fire. All dogs evaluated in this study received 153Sm-EDTMP as a primary or adjunctive treatment at a target dose of 1.0 mCi/kg (37 MBq/kg). Of the 20 dogs evaluated,
7 (35%) had OSA and 13 (65%) had MLO. Tumor locations included the occipital and frontal bones (n = 10 [50%]), zygomatic arch and maxilla region (6 [30%]), palate (3 [15%]), and mandible (1 [5%]).

Of the 20 dogs, 9 were castrated males, 4 were sexually intact males, 3 were sexually intact females, and 4 were spayed females. Eleven of the 20 dogs were < 7 years of age, and 9 were ≥ 7 years of age, with a median age of 8 years (range, 1 to 13 years) for all dogs. There were 12 purebred dogs and 8 mixed-breed dogs. Of the 12 purebred dogs, there were 4 Labrador Retrievers, 3 German Shepherd Dogs, and 1 each of Belgian Malinois, Mastiff, Dalmatian, Old English Sheepdog, and Brittany. Three dogs weighed < 25 kg, and 17 dogs weighed ≥ 25 kg, with a median weight of 33.5 kg (73.7 lb; range, 8.4 to 45.3 kg [18.48 to 99.66 lb]) for all dogs.

Preexisting clinical signs or concurrent illness were reported in 11 dogs and included ≥ 1 of the following: hyperadrenocorticism, hypoadrenocorticism, hypothyroidism, ptalism, episcleritis, lenticular sclerosis, enopthalmus, epiphoria, exophthalmus, and conjunctivitis. In the dogs evaluated, hyperadrenocorticism, hypoadrenocorticism, hypothyroidism, and lenticular sclerosis were thought to be concurrent illness unrelated to tumor burden. However, ptalism, episcleritis, enopthalmus, epiphoria, exophthalmus, and conjunctivitis were considered to be tumor-related changes. Nine dogs were reported to have or develop ocular involvement, whereas 6 did not have evidence of ocular involvement. Ocular condition was not recorded in the remaining patients evaluated. Prior to treatment with 153Sm-EDTMP, of the 20 dogs with complete follow-up data, 13 received previous treatment modalities, including surgery, radiation, chemotherapy, or a combination thereof. Five dogs had no previous treatment, and 2 had no record of the presence or absence of previous treatment. No dogs received surgery, radiation, chemotherapy, or a combination thereof after treatment with 153Sm-EDTMP. However, most patients did continue receiving various combinations of previously prescribed supportive medications. Supportive medications included NSAIDs, prednisone, antimicrobials, an opioid, an H1-receptor antagonist, and antiemetics. Results of statistical analysis indicated no significant correlation between the presence of preexisting clinical signs or concurrent illness (P = 0.242), previous treatments (P = 0.743), age of the dog (P = 0.694), tumor type (P = 0.335), tumor location (P = 0.972), or sex of dog (P = 0.566) in relation to overall survival time (Table 1; Figure 1).

On the basis of radiographic findings, metastasis was suspected in 1 dog, whereas 16 dogs had no evidence of metastasis. Records from 3 dogs included in the study did not provide indication of the presence or absence of metastatic disease. The animal that developed metastatic disease was a castrated male with a diagnosis of MLO of the occipital and frontal bones. The dog developed radiographic evidence of pulmonary metastasis 229 days following treatment; its overall survival time from injection to death was 305 days.

The date of diagnosis and the date of 153Sm-EDTMP injection were obtained and compared among 18 of the 20 dogs. Two of the 20 dogs were excluded because of an inability to establish the date of diagnosis. Of the 18 dogs evaluated, there was a minimum of 3 days, maximum of 195 days, median of 26.5 days, and mean of 47.3 days between the time of diagnosis and the date of 153Sm-EDTMP injection. As stated previously, dogs were grouped into 3 categories according to duration between diagnosis and treatment (1 to 25 days, 26 to 50 days, and ≥ 51 days following diagnosis). Dogs in the 1 to 25 days category had an MST of 105 days. Dogs

Table 1—Comparison of MST for dogs with OSA or MLO of the skull treated with 153Sm-EDTMP on the basis of preexisting clinical signs or concurrent illness, previous treatments, age, tumor type, sex, and tumor location.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of dogs</th>
<th>MST (d)</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>Preexisting clinical signs or concurrent illness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11</td>
<td>105.00</td>
<td>0.242</td>
</tr>
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<td>4</td>
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<td>Previous treatments</td>
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<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12</td>
<td>105.00</td>
<td>0.743</td>
</tr>
<tr>
<td>No</td>
<td>5</td>
<td>128.00</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7 y</td>
<td>11</td>
<td>150.00</td>
<td>0.694</td>
</tr>
<tr>
<td>≥ 7 y</td>
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<td>144.00</td>
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<tr>
<td>Tumor type</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>OSA</td>
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<td></td>
</tr>
<tr>
<td>MLO</td>
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<td>150.00</td>
<td>0.535</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Castrated male</td>
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<td>128.00</td>
<td>0.566</td>
</tr>
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<td>Sexally intact male</td>
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<td>Spayed female</td>
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<tr>
<td>Sexually intact female</td>
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<td>180.00</td>
<td></td>
</tr>
<tr>
<td>Tumor location</td>
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<td></td>
<td></td>
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<tr>
<td>Occipital or frontal bones</td>
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<td>0.972</td>
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<tr>
<td>Zygomatic arch or maxilla</td>
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<td>104.00</td>
<td></td>
</tr>
<tr>
<td>Palate</td>
<td>3</td>
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<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>1</td>
<td>144.00</td>
<td></td>
</tr>
<tr>
<td>Occipital or frontal bones</td>
<td>10</td>
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<td>0.873</td>
</tr>
<tr>
<td>Other bones of the skull</td>
<td>10</td>
<td>128.00</td>
<td></td>
</tr>
</tbody>
</table>

Values of P < 0.05 were considered significant.

Figure 1—Kaplan-Meier survival analysis of the overall survival times of 20 dogs with OSA or MLO treated with 153Sm-EDTMP, comparing tumors affecting the occipital and frontal bones of the skull (solid lines) with those found in other locations of the skull (dashed lines).
in the 26 to 50 days category had the longest MST (169 days), and dogs in the ≥ 51 days category had an MST of 20 days. Kaplan-Meier proportional hazards survival analysis revealed no significant (P = 0.062) difference among the 3 groups.

Overall survival time was calculated by use of the date of 153Sm-EDTMP injection and the date of death. Survival times ranged from 3 to 1314 days, with a mean of 266 days and median of 144 days. One dog was alive at the time of evaluation, with a survival time of 171 days. This dog was censored from the analysis.

Discussion

The results of the present study, with subjective improvement in 4 patients and a lack of clinical evidence of adverse effects, suggest that 153Sm-EDTMP injection may be an option for the treatment of MLO or OSA of the skull in dogs in which other treatments have failed or where surgery is not possible. To our knowledge, this study marks the largest number of dogs with primary bone tumors of the skull and axial bone tumors treated with 153Sm-EDTMP. Previous reports have included only single case reports or smaller series of dogs with primary bone tumors of the skull in which 153Sm-EDTMP treatment was used. In a prior retrospective study of 35 dogs with primary bone tumors treated with 153Sm-EDTMP, 3 axial tumors were found, but only 1 involved the skull. This dog had a mandibular mass, but response to treatment was not assessed in dogs with axial tumors; therefore, individual case outcome could not be ascertained from data provided in that study. Previous publications support the use of 153Sm-EDTMP in dogs with primary bone tumors of the skull that are found to be unsuitable candidates for accepted treatment modalities. Previous reports have indicated that heavy lesion ossification, such as is seen with many tumors of the skull, is a positive predictor for clinical response to 153Sm-EDTMP. Lattimer et al reported that axial lesions have an improved response to treatment. In that study, 2 patients were considered to be cured of disease; 1 of those patients had a mandibular OSA and, despite severe destruction of the bone, had complete involution of the lesion following 153Sm-EDTMP treatment. In a study by Aas et al, 15 dogs treated with 153Sm-EDTMP were evaluated; however, only 2 patients had tumors that involved bones of the skull. In that study, 1 of the 2 skull tumors was a chondroblastic OSA of the maxilla treated with hemimaxillectomy and 153Sm-EDTMP. This patient was free of disease for 4 years after the treatment. In a case report by Moe et al, a single dog with a recurrent OSA of the maxilla was treated with an incomplete surgical excision and adjunctive 153Sm-EDTMP. At 21 months after treatment, reevaluation demonstrated neither relapse nor metastasis. Although it is impossible to say that the patient was cured at only 21 months, and considering that treatment decisions should not be made on the basis of these findings, the overall long-term survival of a patient with maxillary OSA could support a potential benefit of 153Sm-EDTMP treatment.

In early reports of 153Sm-EDTMP use in dogs, Lattimer et al reported that metastatic lesions and axial lesions generally respond well. In the studies by Aas et al and Moe et al, it was reported that 153Sm-EDTMP treatment prevented or at least slowed the growth of OSA metastasis. On the basis of radiographic findings, pulmonary metastasis was suspected in only 1 dog in the present study after incomplete excision of an MLO of the occipital bone. This dog developed metastatic disease 229 days following treatment. The dog survived for 305 days, dying approximately 2.6 months following the development of metastasis. Metastasis was not documented in any of the patients with primary skull OSAs. This sizable cohort of dogs provides strong support to the previous smaller studies in which primary bone tumors of the skull treated with 153Sm-EDTMP have demonstrated low metastatic rates and highlights the potential beneficial effects of 153Sm-EDTMP at reducing the development of metastases.

In the present study, of the 20 tumors evaluated, 13 were determined to be MLOs and 7 were found to be OSAs. Although MST did not differ significantly between tumor types (OSA, 105 days; MLO, 150 days), the range of survival times for dogs with OSA was wide. One dog with an OSA of the occipital protuberance sur-
vived for only 3 days following treatment, whereas a dog with an OSA of the zygomatic arch survived the longest of any dog in the study (1,314 days). A larger study population would be required to determine whether a significant difference in survival time among dogs with OSA and dogs with MLO of the skull exists. The absence of clinically notable metastasis in the long-term surviving OSA patients does suggest a potential difference in the biological behavior of OSA of the skull, compared with appendicular OSA in dogs. Because of the small number of long-term survivors in the present study, a larger study population would also be required to determine whether a significant difference in biological behavior exists.

Multilobular osteochondrosarcomas are slow-growing, locally invasive tumors, with a low overall metastatic rate.\textsuperscript{11,13,14} Metastatic disease found with MLO is slow to occur and is more likely in dogs that have incomplete surgical resection of their primary MLO.\textsuperscript{11} Osteosarcoma is generally a locally invasive tumor with high metastatic potential; however, results of previous studies\textsuperscript{1,2,18,19} have indicated that OSA of the axial skeleton, including tumors of the mandible and maxilla, have a decreased metastatic potential and overall better prognosis, compared with OSA of the appendicular skeleton. Results from those previous studies\textsuperscript{2,9,15} also indicate that OSAs of the appendicular skeleton carry approximately a 90% potential for metastatic disease, whereas results of other reports\textsuperscript{9,9} indicate that only a 34% to 38% prevalence of metastatic disease is associated with OSA of axial locations. In a retrospective study\textsuperscript{6} of 116 dogs with OSA affecting any axial location, pulmonary metastasis was evident on the initial thoracic radiographs in only 11.1% of the dogs. After reviewing the records for the dogs in the present study with OSA of the skull, we speculate that the metastatic rate for skull OSA is significantly less than that for appendicular OSA and perhaps less than the metastatic rate of other axial OSAs in general, although further testing of this hypothesis with a larger study population is needed.

Dogs in the present study were classified into 4 groups by tumor locations: the occipital and frontal bones, zygomatic arch and maxilla region, palate, and mandible. Tumors involving the occipital and frontal bones of the skull were combined into a single category because of suspected similar biological behavior, close bone proximity, and cases of overlapping bone involvement. Outcome was also compared between dogs with tumors of the occipital and frontal bone tumors and those with skull tumors of any other location. Tumor location did not have a significant impact on survival time for dogs in the present study. A previous report\textsuperscript{15} and our clinical experience suggest that the biological behavior of primary bone tumors may vary by location on the skull, with tumors of the mandible thought to be associated with longer MSTs. This was not demonstrated in the present study; however, only 1 tumor was located on the mandible. Tumor location may also influence outcome with regard to likelihood of incomplete resection and metastatic disease. Surgical excision is often a viable and appropriate treatment option for patients with tumors of the skull; however, feasibility of surgery can vary greatly depending on the location of the mass and the structures that are involved. Contrast-enhanced CT with 3-D reconstruction and MRI should be used for visualization of tumor margins, adjacent vital structures, and the overall extent, shape, dimensions, and characteristics of the tumors.\textsuperscript{4,12} When possible, CT and MRI should be performed prior to surgical planning for tumor removal.\textsuperscript{11} Computed tomography and MRI provide differing benefits when evaluating tumors of the head. For tumors of the skull, CT with 3-D reconstruction will provide an increased spatial resolution, excellent bone density imaging, and overall faster imaging time, with a more widespread availability and lower cost. Magnetic resonance imaging provides generally superior intrinsic contrast resolution, generating a greater contrast among adjacent soft tissue structures.\textsuperscript{20,21} Magnetic resonance imaging can be extremely beneficial when evaluating tumor association among surrounding structures as well as possible secondary infection or abscess formation. Ideally, both imaging modalities should be utilized when considering surgical excision. Increased anesthesia time for MRI, patient risk factors, and cost to the owner are considerations. If surgery is attempted, wide surgical margins should be the primary consideration.\textsuperscript{22} Incompletely resected MLOs have previously been reported to have an increased rate of recurrence and metastasis.\textsuperscript{11,13,14} A study\textsuperscript{11} of 16 dogs with MLO demonstrated that 75% of dogs that underwent complete surgical excision did not develop metastasis, whereas 86% of dogs with local recurrence developed metastatic disease. Another study\textsuperscript{15} evaluating dogs with MLO reported an approximate 11-fold increased chance of significantly shorter time to local recurrence with incomplete surgical margins, compared with dogs with complete surgical margins. Osteosarcoma of the skull is likewise a locally invasive tumor, and treatment should also be focused on preventing further local invasion into vital structures. Surgical excision is the treatment of choice to remove the existing mass and prevent further invasion; however, similar to MLO, studies\textsuperscript{1,2,18,19} have shown that prognosis decreases and reoccurrence rates increase with the inability to gain complete excisional margins with OSA. Resection of a minimum of 1 cm of normal tissue surrounding the excised skull tumor is recommended.\textsuperscript{9,15} The present study as well as previous studies\textsuperscript{3,4,10} provides evidence that 153Sm-EDTMP should be considered as a viable treatment option in patients in which surgical resection is not possible because of tumor size or location.

In the present study, no significant age or breed predilection was noted among the population evaluated. There was an overrepresentation (17 [85%] dogs) among dogs ≥ 25 kg. These findings are consistent with those of previous studies\textsuperscript{6,7,11–13} on the typical signalment of dogs with MLO and OSA. Seventeen of the 20 dogs were > 25 kg, which supports previous findings\textsuperscript{6,7,11–13} and indicates a predominance of MLO and OSA in medium- to large-breed dogs. Combining the sexually intact male and castrated male population in the present study resulted in 13 of 20 dogs. Although there was an overrepresentation among male dogs ≥ 25 kg, there was no significance found among sexes. However, this lack of significance could be attributed to an overall small study population. Dates of diag-
nosis, $^{153}$Sm-EDTMP treatment, and death were determined for the dogs evaluated. The time period between date of diagnosis and date of treatment did not appear to have a significant impact on the overall MST. It is unknown how factors such as tumor location, tumor type, tumor size, or tumor growth rate influence the significance for minimizing the time period between diagnosis and treatment. Although it seems clinically prudent not to delay treatment with $^{153}$Sm-EDTMP in appropriately selected patients, prolonged time periods between diagnosis and treatment did not negatively impact outcome for the dogs in the present study.

Variables, including the effect of previous treatment, presence of concurrent illness, and presence of ocular involvement, were evaluated as potential pretreatment prognostic factors, and subjective improvement of dogs 21 days following treatment was examined as a postinjection predictor of prognosis. No correlation was demonstrated between the MST following injection and any of the preinjection or postinjection prognostic factors evaluated. The lack of statistical significance is not necessarily evidence that these factors do not play an important role in the overall prognosis for dogs receiving $^{153}$Sm-EDTMP but may instead be related to the small study population.

The potential limitations of the present study are related to its retrospective nature. Cases were collected over a prolonged period of time, which can lead to an inconsistency in individual patient data. The measurement of hematologic and clinical chemistry variables prior to and after treatment was not able to be documented in all cases; however, $^{153}$Sm-EDTMP treatment was well tolerated with no clinically important adverse events documented. As with previous $^{153}$Sm-EDTMP studies, MRI after treatment was uncommon and therefore did not allow objective response criteria to be used after $^{153}$Sm-EDTMP treatment. Subjective improvement and survival time were used, and in all cases, it was believed that patients were euthanized when pain was no longer controlled or disease progression occurred. Because of the retrospective nature, it was not possible in all cases to document whether the subjective improvement was the attending clinician’s opinion or the owner’s impression. An attempt was made in the present study to use consistent response criteria; however, owing to a lack of criteria consistency in the literature, care should be used when comparing the response among the present study population with that in other studies. Dogs in the present study had a mean survival time of 266 days and an MST of 144 days (approx 4.8 months), with a wide range of survival times (3 to 1,314 days). Given the great variability in outcome, it is clinically important to determine criteria by which one can predict general prognosis and anticipated survival time of dogs that will be treated with $^{153}$Sm-EDTMP.

The variables evaluated in the present study did not predict case outcome relative to overall survival times. The present study provides a foundation for future research on the use of $^{153}$Sm-EDTMP for the treatment of dogs with primary bony tumors of the skull. Prospective evaluation of dogs treated with $^{153}$Sm-EDTMP in the future should include additional factors such as tumor grade and tumor volume relative to skull size.

References