Primary Appendicular Bone Tumors in Dogs

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ABSTRACT: The four common primary appendicular bone tumors in dogs are osteosarcoma, fibrosarcoma, chondrosarcoma, and hemangiosarcoma. The tentative diagnosis of a primary bone tumor is based on signalment, history, clinical signs, and radiographic findings. A definitive diagnosis is obtained from histopathologic evaluation of biopsy specimens. A thorough patient evaluation, including a minimum database, thoracic radiography, and orthopedic and neurologic examination, is necessary to identify concurrent disease, which may alter treatment options. Treatment for all primary bone tumors is aimed at surgical control of the primary tumor and adjuvant chemotherapy for metastatic disease. Appropriate pain management, including narcotic analgesia and palliative radiation therapy, is necessary for dogs that are not candidates for surgical treatment.

Osteosarcoma, chondrosarcoma, fibrosarcoma, and hemangiosarcoma are the most common primary bone tumors of the canine appendicular skeleton. Osteosarcoma is the most common, representing approximately 85% of all primary bone tumors in dogs. Less common are chondrosarcoma (approximately 10%), fibrosarcoma (approximately 5%), and hemangiosarcoma (approximately 5%). The prognosis for all dogs with primary bone tumors is guarded, especially for those with osteosarcoma and hemangiosarcoma, which readily metastasize. Treatment for primary bone tumors generally consists of surgery to control the spread of the primary tumor followed by adjuvant chemotherapy. Palliative radiation therapy and narcotic analgesics may benefit dogs that are not surgical candidates.

SIGNALMENT

Canine appendicular osteosarcoma most commonly affects large and giant breeds. German shepherds, Great Danes, Labrador retrievers, Saint Bernards, and rottweilers are overrepresented in most studies and may not be representative of the overall population. Male dogs are predisposed to develop osteosarcoma, except in the case of Saint Bernards where females are at increased risk. The mean age at diagnosis for canine osteosarcoma is 8 years, but there is a distinct peak in incidence at 18 to 24 months. Chondrosarcoma most commonly develops in the axial skeleton of large- and medium-breed dogs, German shepherds, boxers, golden retrievers, and mongrels are commonly affected. Unlike osteosarcoma, chondrosarcoma rarely occurs in giant-breed or small (less than 18 kg [40 lb])
dogs. The mean age at diagnosis for canine appendicular chondrosarcoma is 6 years, and there is no reported sex predilection. The mean age of dogs diagnosed with primary appendicular fibrosarcoma is 8.4 years. This type of tumor usually occurs in medium- to large-breed dogs with no reported sex predilection. The mean age of dogs affected with appendicular hemangiosarcoma is 7 years. Hemangiosarcoma of the bone most commonly affects German shepherds, boxers, and Great Danes.

**HISTORY AND CLINICAL SIGNS**

Lameness is the most common presenting sign in dogs with primary bone tumors. In some dogs, mild trauma is associated with the initial observation of lameness. This often leads to a misdiagnosis of a strain or sprain. The lameness is intermittent and mild initially but progresses to become persistent and severe. Lameness associated with primary bone tumors is likely due to either the presence of microfractures or disruption and stretching of the periosteum. Dogs may also develop an acute non-weight-bearing lameness resulting from a pathologic fracture. Muscle atrophy of the affected limb may be noted and is secondary to the persistent lameness; therefore, complete neurologic and orthopedic examinations are necessary to identify concurrent orthopedic or neurologic diseases (e.g., hip dysplasia, degenerative myelopathy) that might affect treatment options.

**RADIOGRAPHY**

Good-quality orthogonal radiographs of the affected bone are important for evaluating suspected bone tumors (see box below). Cortical lysis is a common early radiographic feature, and some primary bone tumors have a characteristic sunburst appearance radiating from areas of cortical destruction. As the tumor invades the cortex, the periosteum becomes elevated and new bone is deposited, forming a triangular structure known as Codman’s triangle. The presence of Codman’s triangle is, however, not pathognomonic for primary bone tumors. Radiographically evident soft tissue swelling associated with the tumor may be present in some dogs.

Appendicular osteosarcoma occurs most commonly in the metaphyseal region of the long bones and tends not to cross joints. In dogs, 47% of osteosarcomas develop in the forelimb, whereas 29% occur in the pelvic limb. The most common sites affected are the distal radius (23%; Figure 1), proximal humerus (19%), distal femur (14%), and proximal (9%) and distal (7%) tibia. Although fibrosarcoma occurs more commonly in the axial skeleton, when it develops in the appendicular skeleton of dogs it affects the bony metaphysis. Appendicular hemangiosarcoma is most commonly diagnosed in the proximal humerus.

**DIAGNOSTIC DIFFERENTIALS**

Although osteosarcoma is the most likely clinical diagnosis for an older dog with a radiographically apparent metaphyseal lesion, diagnostic differentials include other primary bone tumors, metastatic tumors, and bacterial or fungal osteomyelitis. The most common fungal organisms affecting bone are *Coccidioides immitis* and *Blastomyces dermatitidis*; dogs with systemic mycotic infections are usually clinically ill. Bacterial osteomyelitis is typically associated with penetrating trauma, such as a dog bite, deep laceration, puncture wound, or open fracture. Although geographic location, travel to endemic fungal areas, previous trauma, febrile illness, and patient signalment offer additional clues as to the clinical diagnosis, a bone biopsy with histopathology and possibly culture is the only way to establish a diagnosis.
definitive diagnosis. Serology may be helpful in identifying fungal disease, particularly coccidioidomycosis.

Tumors that metastasize to bone include carcinoma of the mammary gland, prostate, lung, liver, nasal cavity, or urinary bladder; squamous cell carcinoma; and synovial cell sarcoma. Compared with primary bone tumors, metastatic tumors are often polyostotic, are located within the diaphysis, and have less radiographic evidence of cortical destruction; however, a biopsy is necessary to confirm the diagnosis.

**BIOPSY**

Tissue specimens from a suspected primary bone tumor can be collected using several methods. Fine-needle aspiration is a minimally invasive technique used to obtain cytology specimens and may provide a rapid diagnosis. Ultrasonography increases the likelihood of collecting a diagnostic sample by guiding the needle through thin or disrupted areas of bone cortex. Bone cytology specimens are processed routinely for microscopic examination; however, histopathology is still necessary for a definitive diagnosis.

The most effective instruments for collecting bone biopsy specimens include the Jamshidi bone biopsy needle and the Michel trephine. The biopsy needle is inserted into the bone through a small stab incision (closed technique). The Michel trephine collects large bone specimens that are likely to identify a tumor; however, the larger biopsy sites may increase the risk of pathologic fracture. The Jamshidi needle (Figure 2), which is smaller than the Michel trephine, is used to collect samples that are sufficient to distinguish tumor from nontumor pathology in more than 90% of cases, which is slightly lower than when using the Michel trephine. Using these bone biopsy needles, a solid bone core is collected from the radiographic center of the tumor, extending to but not penetrating the far cortex. To enhance diagnosis, the biopsy needle should be redirected so multiple samples can be obtained. Alternatively, a surgical approach can be made to the bone lesion and the biopsy specimen can be collected with rongeurs (open technique). Open bone biopsy procedures are associated with greater risk of wound dehiscence, infection, drainage, and pathologic fractures compared with needle biopsies. Both open and closed biopsies should be performed while the patient is anesthetized, using strict aseptic techniques.

Depending on where within the lesion the biopsy is taken, the specimen may contain only reactive bone, and the owner should be forewarned about this possibility. Collecting multiple biopsy specimens from a lesion may improve the chances of making a diagnosis. Tumor seeding is a potential complication with any biopsy technique but is especially important when the owner is considering limb-sparing surgery. In this situation, the biopsy should be taken by the surgeon who will perform the limb-sparing procedure. If the biopsy results will not affect the dog’s treatment, then amputation or limb-sparing surgery can be performed as both a therapeutic and diagnostic procedure. After definitive surgical treatment, the affected bone must always be submitted for histopathologic evaluation to establish a diagnosis or to confirm the results from the needle biopsy.

**STAGING**

All dogs with primary bone tumors should undergo thorough clinical staging, including biopsy, to evaluate the extent of their disease (see box below). In addition to clinical staging, dogs with primary bone tumors should be carefully evaluated for the presence of neurologic and orthopedic diseases. Thoracic radiography and nuclear scintigraphy are useful for

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**Classification and Staging of Canine Primary Bone Tumors**

<table>
<thead>
<tr>
<th>Tumor Classification</th>
<th>Staging</th>
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<tbody>
<tr>
<td><strong>Primary tumor (T)</strong></td>
<td><strong>Stage I:</strong> G₁, M₀</td>
</tr>
<tr>
<td>T₀ = No evidence of tumor</td>
<td><strong>Stage II:</strong> G₂, M₀</td>
</tr>
<tr>
<td>T₁ = Tumor confined to the medulla and cortex</td>
<td><strong>Stage III:</strong> G₁ or G₂, M₁</td>
</tr>
<tr>
<td>T₂ = Tumor extends beyond the periosteum</td>
<td><strong>Substage a:</strong> T₁</td>
</tr>
<tr>
<td><strong>Metastasis (M)</strong></td>
<td><strong>Substage b:</strong> T₂</td>
</tr>
<tr>
<td>M₀ = No evidence of metastasis</td>
<td><strong>G = histologic grade; G₁ = low grade; G₂ = high grade.</strong></td>
</tr>
<tr>
<td>M₁ = Metastasis detected</td>
<td><strong>M₀ = No evidence of metastasis</strong></td>
</tr>
</tbody>
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**Figure 2**—A Jamshidi needle is used for collecting bone core specimens of suspected tumors for histopathology.
identifying metastatic disease. Up to 10% of dogs with osteosarcoma have identifiable pulmonary or skeletal metastases at presentation. Negative findings from thoracic radiographs or nuclear scintigraphy, however, should not exclude the possibility of occult metastatic disease. A complete blood cell count (CBC), serum biochemistry profile, and urinalysis should be performed to assess the general health of the patient and to evaluate the anesthetic risks. Most dogs are initially diagnosed with stage IIb cancer.

**TREATMENT**

The treatment of primary bone tumors is aimed at local control of the tumor, prevention or delay of metastatic disease, and palliation of clinical signs. Local tumor control is accomplished by surgical removal of the affected bone; systemic chemotherapy is used to address metastatic disease; and analgesics and radiation therapy may be used to palliate clinical signs in dogs that are not surgical candidates.

**Amputation**

Amputation is the most common surgical treatment for dogs with primary bone tumors. Most owners are pleased with the results of amputation and the dogs ambulate comfortably. Amputation removes the risk of pathologic fracture and the source of chronic pain. Thoracic limb amputation is best accomplished by forequarter amputation. Pelvic limb amputation by coxofemoral disarticulation is preferred, except when the tumor affects the proximal femur or pelvis. In these dogs, a partial or complete hemipelvectomy may be required for a complete surgical excision. After amputation, the prognosis for appendicular chondrosarcoma and fibrosarcoma is good, and affected dogs are potentially cured if the entire tumor can be removed because of the relatively low metastatic rate of these tumors. Median survival times for dogs with appendicular chondrosarcoma treated with amputation alone range from 201 to 540 days. Appendicular fibrosarcoma is typically a slow-growing tumor that is locally invasive and rarely develops metastases. Prognosis is good with complete resection, with reported survival times up to 72 months after amputation alone. Osteosarcoma and hemangiosarcoma have a high potential for metastasis, which warrants adjuvant chemotherapy. Therefore, amputation should be considered a palliative treatment for dogs with osteosarcoma or hemangiosarcoma.

**Limb Sparing**

Limb sparing involves surgical removal of the affected bone, replacement with a cortical allograft,
bone plate application, and arthrodesis of the adjacent joint.\textsuperscript{2,5,6,19,22} Limb sparing is indicated for dogs that will not function well after amputation (e.g., giant-breed dogs, dogs with severe orthopedic or neurologic disease) and for dogs whose owners absolutely refuse amputation.\textsuperscript{1,2,5} Dogs must be carefully chosen for limb-sparing surgery. Commonly used criteria include a tumor that involves less than 50% of the bone radiographically, no demonstrable metastatic disease, and otherwise good patient health.\textsuperscript{19} Currently, limb sparing is only recommended for dogs with primary bone tumors of the distal radius and ulna.\textsuperscript{19} Other sites, including the proximal humerus, distal femur, and proximal and distal tibia, are not well suited for limb sparing because of increased infection rates and poor limb function.\textsuperscript{2,17} Dogs function well after distal radius and ulna limb-sparing procedures.\textsuperscript{19}

Postoperative infection occurs in approximately 40% of dogs undergoing limb-sparing surgery.\textsuperscript{2,17,23} Predisposing factors include the implantation of a large nonvascular allograft, extensive soft tissue dissection at the surgical site, sparse soft tissue overlying the surgical site, and immunosuppression associated with chemotherapy.\textsuperscript{7} However, dogs that develop infection enjoy significantly longer survival times than dogs that do not develop infection.\textsuperscript{23} Infection may be controlled in up to 75% of cases with long-term antibiotic therapy selected on the basis of bacterial culture and sensitivity; some dogs require lifelong antibiotic therapy. For refractory infections, implantation of antibiotic-impregnated beads, removal of the allograft, or amputation may be necessary.\textsuperscript{1,17,24}

Local tumor recurrence is a devastating complication that occurs in 15% to 25% of dogs that undergo limb-sparing surgery.\textsuperscript{23} Various methods, including preoperative chemotherapy, implantation of an open polylactic-acid sponge containing cisplatin, and intraoperative radiation therapy have been used to minimize local recurrence.\textsuperscript{1,2,17,23} A new technique for limb sparing, whereby the tumor is removed by en bloc resection, has been described. An osteotomy is made in the bone and is slowly distracted with a circular external fixator until bony union occurs. This process, called distraction osteogenesis,\textsuperscript{17} is a salvage procedure for severe cases of osteomyelitis.\textsuperscript{17}

Chemotherapy

Dogs with appendicular osteosarcoma clearly benefit from adjuvant chemotherapy.\textsuperscript{2,19} Multiple chemotherapy regimens have been shown to prolong median survival times of dogs with osteosarcoma treated surgically with amputation or limb sparing.\textsuperscript{2,13,17} Chemotherapy drugs commonly used to treat osteosarcoma include cisplatin (Platinol\textsuperscript{®}, Bristol-Myers Squibb, Princeton, NJ), carboplatin (Paraplatin\textsuperscript{®}, Bristol-Myers Squibb), and doxorubicin (Adriamycin\textsuperscript{®}, Adria Laboratories, Columbus, OH). The role of chemotherapy in the management of the other primary appendicular bone tumors is unknown.\textsuperscript{2,4,12} Because of the highly metastatic nature of hemangiosarcoma, however, adjuvant chemotherapy may be warranted. Even with adjuvant chemotherapy using a combination of doxorubicin, vincristine, and cyclophosphamide, only 10% of dogs with soft tissue hemangiosarcoma survive 1 year.\textsuperscript{2}

Cisplatin is a heavy metal compound used as either a single agent or in combination with doxorubicin for the treatment of osteosarcoma.\textsuperscript{6,7} Adverse effects of cisplatin therapy include nephrotoxicity, gastrointestinal toxicity, and myelosuppression. Nephrotoxicity can be prevented with aggressive saline diuresis 4 hours before and 2 hours after cisplatin infusion. Emesis during drug infusion can be prevented with butorphanol; however, prolonged anorexia may be more difficult to treat. A CBC should be taken before each dose of cisplatin; dogs with a neutrophil count less than 3000/µl should not be given cisplatin chemotherapy until their bone marrow recovers.\textsuperscript{2} Cisplatin is given intravenously once every 3 weeks for a total of two to nine doses.\textsuperscript{2,9}

Carboplatin is a second-generation platinum drug that has fewer renal and gastrointestinal adverse effects than cisplatin. Its dose-limiting toxicity is myelosuppression. Carboplatin chemotherapy in dogs with osteosarcoma results in similar survival times to those

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose/Route</th>
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<tbody>
<tr>
<td>Fentanyl</td>
<td>For dogs weighing:</td>
</tr>
<tr>
<td>- &lt;10 kg = 25 µg/kg/hr transdermally</td>
<td></td>
</tr>
<tr>
<td>- 10–20 kg = 50 µg/kg/hr transdermally</td>
<td></td>
</tr>
<tr>
<td>- 21–30 kg = 75 µg/kg/hr transdermally</td>
<td></td>
</tr>
<tr>
<td>- &gt;30 kg = 100 µg/kg/hr transdermally</td>
<td></td>
</tr>
<tr>
<td>Sustained-release morphine</td>
<td>0.3 to 3.0 mg/kg q8–12h PO</td>
</tr>
<tr>
<td>Codeine + acetaminophen</td>
<td>1 to 2 mg/kg (based on codeine) q4–6h PO</td>
</tr>
<tr>
<td>NSAIDs\textsuperscript{a}</td>
<td></td>
</tr>
<tr>
<td>- Carprofen</td>
<td>2.2 mg/kg q12h PO</td>
</tr>
<tr>
<td>- Aspirin</td>
<td>5 to 10 mg/kg q12h PO</td>
</tr>
<tr>
<td>- Piroxicam</td>
<td>0.3 mg/kg/day PO</td>
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\textsuperscript{a}NSAIDs will not provide enough pain alleviation in most cases.
in dogs treated with cisplatin chemotherapy. The primary advantage of carboplatin over cisplatin is its ease of administration because diuresis and antiemetic therapy are not required.

Doxorubicin, an antitumor antibiotic used for the treatment of many cancers, is used as a single agent or in combination with cisplatin for the treatment of osteosarcoma. Doxorubicin is cardiotoxic, and the total cumulative dose should not exceed 240 mg/m². The agent may also cause vomiting or diarrhea. Doxorubicin must be given intravenously with care; drug extravasation can result in catastrophic tissue sloughing and hypersensitivity reactions can occur during drug infusion. Use of generic doxorubicin is associated with increased incidence of hypersensitivity reactions in dogs.

Palliation

For some dogs, aggressive surgical and medical treatment of primary bone tumors is not possible due to the presence of concurrent disease or the owner's financial limitations. In these cases, palliative treatment is appropriate if the owner is not prepared to consider euthanasia. As mentioned previously, amputation as the sole treatment for highly metastatic primary bone tumors, such as osteosarcoma and hemangiosarcoma, is considered palliative treatment, providing several months of pain-free life after recovery from surgery. Alternatively, external-beam radiation therapy is an effective method for relief of pain associated with appendicular osteosarcoma in dogs. Dogs should receive three radiation treatments of 8 to 10 Gy each on days 0, 7, and 21. Up to 70% of treated dogs have pain relief lasting more than 2 months. The radionucleotide therapy samarium may be useful in the relief of some pain associated with the primary osteosarcoma or its metastasis. The effect of radiation on nonosteoid sarcomas of bone is unknown. When surgery or radiation therapy is not a viable treatment option or when an owner needs time to make a decision regarding therapy, medical pain management is appropriate (Table 1). NSAIDs may not provide sufficient analgesia but can be combined with narcotics for better pain control. Transdermal fentanyl or sustained-release morphine is a suitable choice for dogs with primary bone tumors.

METASTASIS

Metastasis is responsible for the death of most dogs with appendicular osteosarcoma. Approximately 90% of dogs with osteosarcoma have micrometastases at the time of diagnosis. The median survival time for dogs with osteosarcoma treated by amputation alone is 134
days, with 11% of treated dogs surviving 1 year and only 2% surviving 2 years (Table 2). The death of these dogs is often due to pulmonary metastasis (Figure 3). Survival rates after radiation therapy alone for the treatment of osteosarcoma are similar. By delaying or preventing the onset of metastatic disease, adjuvant chemotherapy prolongs the median survival times after amputation; however, the increased use of adjuvant chemotherapy increases the frequency of bony metastases. Other potential sites for metastases include intraabdominal organs, the amputation site, regional lymph nodes, and the heart. Hemangiosarcoma is a highly aggressive tumor, and many animals with this type of tumor have metastases at the time of diagnosis. The majority of dogs with appendicular hemangiosarcoma develop metastases within 6 months of diagnosis. Dogs with appendicular hemangiosarcoma should undergo thorough clinical staging because the bony lesion may represent a metastasis from a distant primary tumor.

Pulmonary metastases can be treated surgically with a procedure called pulmonary metastasectomy, whereby a lateral thoracotomy or median sternotomy is performed and the affected areas are removed by partial or complete lung lobectomy. Patients selected for a pulmonary metastasectomy should meet the following criteria: surgical control of the primary tumor, a disease-free interval of at least 12 months, fewer than three radiographically visible lesions, and a metastasis diameter doubling time of more than 40 days. Median survival time of dogs with osteosarcoma treated with pulmonary metastasectomy is 176 days. Chemotherapy has not been effective in causing regression of pulmonary metastases in dogs with osteosarcoma. Intravenous administration of the radioisotope samarium may be useful for the management of both primary and metastatic bone tumors.

### PROGNOSTIC FACTORS

Pretreatment predictors for survival have been identified in dogs with appendicular osteosarcoma. Age and total serum alkaline phosphatase (ALP) activity are predictive of treatment outcome. Dogs younger than 5 years or older than 10 years of age when osteosarcoma is diagnosed have shorter survival times than do dogs diagnosed between the ages of 7 to 10 years. Dogs with total serum ALP activity greater than 110 U/L had a significantly shorter median survival time (177 days) when compared with dogs with total serum ALP activity less than 100 U/L (495 days).

### CONCLUSION

Osteosarcoma, chondrosarcoma, fibrosarcoma, and hemangiosarcoma are the most common primary appendicular bone tumors that occur in dogs. The diagnostic approach and clinical staging procedures for these tumors are the same regardless of the histologic type. The prognosis for all dogs with appendicular bone tumors is guarded; the tumors in dogs with chondrosarcoma and fibrosarcoma have a lower metastatic rate than do those with osteosarcoma and hemangiosarcoma. The best treatment outcome for appendicular bone tumors results from complete resection of the tumor followed by adjuvant chemotherapy.
REFERENCES


1. Often the first clinical sign owners notice in dogs with primary appendicular bone tumors is
   a. soft tissue swelling.
   b. an open, draining wound.
   c. non-weight-bearing lameness.
   d. subtle lameness after mild trauma.
   e. a and b

2. Definitive diagnosis of primary appendicular bone tumors
   a. can be made based on radiographs.
   b. is made histopathologically.
   c. is not needed because all treatments are the same.
   d. is best carried out using open biopsy techniques.
   e. a and c

3. The most common complication after limb sparing is
   a. local tumor recurrence.
   b. infection.
   c. implant loosening/breakage.
   d. renal toxicity due to open polylactic acid sponge.
   e. vomiting.

4. Radiation therapy is used in dogs with appendicular osteosarcoma
   a. to increase survival time, requiring 10 doses of 3 Gy each.
   b. for palliation of pain, requiring two to three doses of 8 to 10 Gy each.
   c. for palliation of pain, requiring a single dose of 70 Gy.
   d. for treatment of pulmonary metastatic lesions, requiring many portals.
   e. for control of soft tissue swelling, requiring 16 doses of 2 Gy each.

5. For a dog to be considered for limb-sparing surgery, what is the upper limit of radiographically affected bone?
   a. 20%
   b. 30%
   c. 40%
   d. 50%
   e. 60%

   a. 5% to 15%
   b. 15% to 25%
   c. 25% to 35%
   d. 35% to 45%
   e. more than 50%

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Primary Bone Tumors (continued from page 138)

7. Which is not a criterion for a patient when considering a metastasectomy?
   a. tumor size d. tumor doubling time
   b. tumor number e. disease-free interval
   c. lung lobe affected

8. A major advantage of carboplatin chemotherapy compared with cisplatin chemotherapy is that carboplatin
   a. does not require extensive saline diuresis for renal protection.
   b. requires extensive diuresis before and after treatment.
   c. causes less nausea and vomiting.
   d. is less expensive.
   e. a and c

9. Which of the following is not a good palliative treatment option for a dog with a primary bone tumor?
   a. external-beam radiation d. amputation
      therapy e. NSAIDs
   b. narcotic analgesics
   c. benign neglect

10. Amputation without chemotherapy is adequate treatment for
    a. chondrosarcoma. d. osteosarcoma.
    b. fibrosarcoma. e. a and b
    c. hemangiosarcoma.