
Holly A. Phelps, DVM; Charles A. Kuntz, DVM, MS, DACVS; Rowan J. Milner, BVSc, MMed Vet, DACVIM; Barbara E. Powers, DVM, PhD, DACVP; Nicholas J. Bacon, MA, VetMB, DACVS

**Objective**—To evaluate outcomes of radical excision of feline injection-site sarcomas (ISS) via assessment of local recurrence and metastasis rates, survival times, and complications associated with surgery.

**Design**—Retrospective case series.

**Animals**—91 cats with ISS.

**Procedures**—Medical records of cats that had radical excision of ISS without adjunctive treatment were reviewed. Information extracted included sex, type of surgical procedure, histologic tumor grade, tumor diameter, time from tumor detection to definitive surgery, complications associated with surgery, whether tumors recurred locally or metastasized, and survival times. Diagnosis of ISS was histologically confirmed, and additional follow-up was performed.

**Results**—Overall median survival time was 901 days. Thirteen of 91 (14%) cats had local tumor recurrence; 18 (20%) cats had evidence of metastasis after surgery. Median survival time of cats with and without recurrence was 499 and 1,461 days, respectively. Median survival time of cats with and without metastasis was 388 and 1,528 days, respectively. Tumor recurrence and metastasis were significantly associated with survival time, whereas other examined variables were not. Major complications occurred in 10 cats, including 7 with incisional dehiscence.

**Conclusions and Clinical Relevance**—Radical excision of ISS resulted in a metastasis rate similar to rates reported previously; the local recurrence rate appeared to be substantially less than rates reported after less aggressive surgeries, with or without adjuvant treatment. Major complication rates were similar to rates reported previously after aggressive surgical resection of ISS. Radical excision may be a valuable means of attaining an improved outcome in the treatment of feline ISS. (J Am Vet Med Assoc 2011;239:97–106)
races and survival times have been documented following various combinations of surgery (marginal vs wide or local vs radical resection), radiation treatment (before or after surgery), and chemotherapy with no reliable difference in outcome reported between various aggressive treatment protocols. In 2 studies, completeness of surgical excision was shown to affect rates of local recurrence, with 58% and 69% recurrence rates associated with incomplete excision versus 19% and 22% associated with complete excision. In addition, complete excision has been associated with a longer time to first recurrence and a longer tumor-free interval (time to first recurrence or metastasis) than has incomplete excision.

Historically, authors of reviews evaluating surgical excision of soft tissue sarcomas in dogs have recommended resection of tumors to include 2- to 3-cm margins laterally and 1 fascial plane deep to the tumor bed. Although this approach has been adopted for the treatment of ISS in cats, it may not be adequate, considering the reported high rates of local recurrence in this species. In response to this, several authors have suggested more radical methods, including surgical margins of \( > 3 \text{ cm} \) laterally and 1 to 2 fascial planes deep to the tumor, along with partial scapulectomy, osteotomy of spinal processes, or hemipelvectomy when indicated.

Currently, the Vaccine-Associated Feline Sarcoma Task Force recommends multimodal treatment, including surgical resection with at least 2-cm margins in all planes, although the use of 3- to 5-cm margins is also considered in the Task Force discussions. However, to the authors’ knowledge, no current studies have evaluated the outcome of consistently performed radical excision without adjuvant treatment for feline ISS.

In the study reported here, we defined radical excision as tumor resection including 5-cm margins surrounding the palpable tumor edge. This included excision of surrounding soft tissue, bone, or body wall; if resection of 2 muscle planes or bone was achievable, 1 fascial plane deep to the palpable tumor, this was considered an acceptable deep margin. The primary objective of this retrospective study was to evaluate the outcome of radical excision of feline ISS in terms of local recurrence rates, metastasis rates, and survival time after surgery without administration of pre- or postoperative adjuvant treatments. A secondary goal was to describe complications associated with radical excision of ISS.

### Materials and Methods

**Criteria for selection of cases**—Hardcopy medical records of cats referred to the Regional Veterinary Referral Center in Springfield, Va, for surgical treatment of soft tissue sarcomas in locations commonly associated with vaccination between December 14, 1998, and November 27, 2002, were reviewed. All cats were privately owned; in addition to surgery, adjunctive pre- or postoperative radiation treatment of cats was offered to owners at the time of evaluation. All cats in the study underwent radical tumor excision as described. All cats included in the study population had 3-view thoracic radiography at the time of presurgical evaluation and had no evidence of pulmonary metastasis. Cats were included if paraffin-embedded tissue sections of the resected tumor were available for histologic analysis and samples were found to be consistent with ISS on the basis of previously described histologic criteria. Cats that had excision of scars from previous surgery were included only if residual tumor cells were detected via histologic examination.

Cats that received radiation treatment or chemotherapy in addition to surgery during the study period were excluded. Cats were also excluded if follow-up time (defined as the number of days after definitive surgery [ie, radical tumor excision at our institution] for which information was available) was less than the shortest time to local tumor recurrence within the population.

**Medical records review**—Information obtained from each record included sex of the cat, type of surgical procedure, histologic tumor grade, tumor diameter, time from tumor detection to definitive surgery, whether tumors recurred locally or metastasized, complications associated with surgery, and survival times (ie, time from definitive surgery until death). Major complications were defined as those requiring additional anesthesia or surgery.

**Surgical procedures and histologic evaluation**—All cats were premedicated with acepromazine \((0.1 \text{ mg/kg} \ [0.05 \text{ mg/lb}], \text{ SC}), \) glycopyrrolate \((0.01 \text{ mg/kg} \ [0.005 \text{ mg/lb}], \text{ SC}), \) and morphine \((0.1 \text{ mg/kg}, \text{ SC}), \) and anesthesia was induced with propofol \((5 \text{ mg/kg} \ [2.27 \text{ mg/lb}], \text{ IV}) \) and maintained with isoflurane in oxygen. All surgeries were performed by 1 board-certified surgeon (CAK). The maximum palpable diameter of the tumor or previous surgical scar was measured and recorded. Hair was clipped over the surgical site, and the skin was aseptically prepared. The extent of the tumor and previous surgical scar was marked with a black, alcohol-based ink marker. The proposed surgical excision line, 5 cm away from the tumor edge or surgical scar, was then drawn on the skin surface. Surgical planning did not include CT or MRI in any cat.

Surgical excision was performed by means of sharp dissection and cautery. The skin was excised along the described marked margins. An adequate deep margin was defined as including 2 muscle planes or bone deep to the tumor. Any anatomic structures that fell within the determined margins were excised, including thoracic wall, abdominal wall, dorsal spinous processes, ilial wing, and scapula. If the tumor was subcutaneous and could be elevated away from underlying structures with 5-cm margins, the underlying structures were not excised. Amputation was performed if tumor excision would significantly impair normal function of a limb. Tumor location and description of surgery were recorded. Surgeries were characterized by location and anatomic structures removed.

Excision of interscapular tumors included osteotomies of the dorsal spinous processes, close to the dorsal lamina of the vertebra if necessary. For interscapular resections where the defect could not be closed through direct apposition of the surgical wound edges, a single-pedicled advancement flap from the caudal dorsal skin was elevated and used for wound closure. Excision methods for tumors overlying the...
scapulpectomy were determined according to location. A partial scapulpectomy was performed in cats with tumors associated with the dorsal scapula, whereas a forequarter amputation including scapulpectomy was performed in cats with more ventrally located tumors.

For tumors of the thoracic wall, rib resection was performed if soft tissue excision alone would not achieve the required deep margin. Removal of tumors closer to dorsal midline included resection of epaxial muscles and osteotomies of the dorsal spinous processes. If the thoracic wall could not be reconstructed by use of local autogenous tissues, polypropylene mesh was used with apposition of muscle over the mesh when possible. Abdominal wall tumors were excised in a similar manner to those of the thoracic wall. Osteotomies of the iliac shaft or wing were performed in cats with lateral pelvic tumors; some required abdominal wall resection on the basis of tumor location. Cats with tumors of the distal thigh underwent limb amputation with coxofemoral disarticulation, whereas those with more proximal thigh masses underwent hemipelvectomy. Some tumors in transitional zones required combinations of surgical techniques.

Polydioxanone suture was used for closure in muscle layers and subcutaneous tissues. Care was taken to anatomically appose incised muscle bodies to allow for hemostasis, improved dead-space closure, and maximal preservation of function. The skin was closed by use of skin staples or nylon suture. Surgical margins were marked with India ink on the cut surface of excised tissues immediately after surgical resection. All tumors were placed in neutral-buffered 10% formalin solution in their entirety and were histologically evaluated by 1 board-certified pathologist (BEP). Slides of all tumors were examined to determine histologic diagnosis, degree of differentiation, tumor grade (I to III) based on previously described guidelines, and completeness of the surgical excision.

Analgesia—Cats that underwent surgical excisions caudal to the L2 vertebral body received preservative-free morphine (0.1 mg/kg) and lidocaine (1 mg/kg [0.45 mg/lb]) via epidural administration prior to surgery. The local tissues were infiltrated with bupivacaine (3 mg/kg [1.36 mg/lb], topically) prior to closure. A constant rate infusion of fentanyl (2.8 µg/kg/h [1.27 µg/lb/h], IV) was administered for 18 to 24 hours after surgery. Concurrently, morphine boluses (0.1 mg/kg, IV) were additionally administered in cats subjectively determined to have signs of pain. Transdermal fentanyl patches (25 µg/h) were placed on the skin for all cats weighing > 2.7 kg (5.94 lb) immediately after surgery. Fentanyl patches were intended to be removed by the owner after 5 to 7 days. For cats weighing < 2.7 kg, codeine elixir (0.5 to 1.0 mg/kg [0.23 to 0.45 mg/lb], PO) was administered every 4 to 6 hours for 3 to 5 days following discharge from the hospital. Cats with fentanyl patches that were subjectively determined to be dysphoric or stuporous were given a dose of naloxone (0.1 mL/cat, IV); if clinical signs were alleviated after naloxone administration, the fentanyl patch was removed and codeine elixir was administered as described.

Follow-up—Thoracic radiography at 3-month intervals was recommended for all cats after surgery, subject to owners’ wishes and compliance. Any pulmonary nodular interstitial or metastatic pattern detected on thoracic radiographs was presumed to be ISS related. Metastasis to locations other than the thorax was confirmed histologically. Any firm mass palpated along the surgical scar by the primary surgeon or referring veterinarian was deemed a local recurrence. Most suspected recurrences were not confirmed cytologically or histologically. Additional follow-up was performed via telephone conversations with each owner or referring veterinarian, and questions regarding local recurrence, metastasis, and death were asked.

Statistical analysis—The RFI was defined as the number of days between definitive surgery and detection of local tumor recurrence. The MFI was defined as the number of days between definitive surgery and evidence of metastasis, and survival time was defined as the number of days between definitive surgery and death. Cause of death was classified as tumor or non–tumor related. Descriptive statistics were calculated, and data were tested for normal distribution and equal variance by means of the Kolmogorov-Smirnov test. Data that were normally distributed are reported as mean ± SD. Data that were not normally distributed are reported as median and IQR, representing the difference between the first and third quartiles. For survival data, 95% CI for the median is reported. Kaplan-Meier survival analysis with the Gehan-Breslow statistic was used for calculation of median survival time, RFI, and MFI and for comparison among the described factors. Any factors considered significant (P < 0.05) via the Gehan-Breslow statistic for RFI, MFI, or survival time were tested for significance via Kruskal-Wallis ANOVA. Multivariate analysis was performed by use of multiple logistic regression to fit the Cox proportional hazards model for survival. For all analyses, values of P < 0.05 were considered significant. Cats that were alive at the end of the study or were lost to follow-up were censored for analysis. Statistical analysis was performed by use of 2 commercial software packages.

Results

Patient information—Records of 147 cats referred for management of ISS were identified, but 56 of these were subsequently excluded; 21 had pre- or postoperative radiation treatment, 5 received adjuvant chemotherapy, 5 had evidence of metastatic disease (including 1 cat that did not have thoracic radiography performed prior to definitive surgery but had pulmonary metastasis detected 12 days after this surgery), and 17 had no treatment. Seven additional cats were excluded because their follow-up periods were less than the shortest RFI within the study population (80 days); 4 of these cats were lost to follow-up (follow-up range, 2 to 77 days), and 3 died. Of the 3 cats that died, 1 died of respiratory arrest (7 days after surgery) and 2 died of non–tumor-related causes (range, 32 to 41 days after surgery). One other cat was excluded because of unknown dates of local tumor recurrence and death.

Ninety-one cats (45 males and 46 females) met the inclusion criteria; all cats were neutered. There were...
86 mixed-breed cats, 3 Siamese, and 1 each of Himalayan and Snowshoe breeds. Mean ± SD age at referral for definitive surgery was 10.1 ± 3.6 years. Seventy-two (79%) cats had no prior surgical treatment, 15 (16%) had 1 previous surgery, 3 (3%) had 2 previous surgeries, and 1 (1%) had 9 previous surgeries for excision of ISS. Median time between initial tumor detection and definitive surgery was 30 days (IQR, 12 to 75 days). The median duration of follow-up was 535 days (IQR, 301 to 1,001 days).

Tumor characteristics—The median maximum tumor diameter was 4 cm (IQR, 3 to 5 cm). Histologic examination confirmed the diagnosis of ISS in all cases. Of 91 tumors, 89 (98%) were FSAs and 2 (2%) were MFHs. Histologic analysis and grading by the pathologist (BEP) revealed that 5 (3%) tumors were grade I, 32 (35%) were grade II, and 54 (59%), including both MFHs, were grade III. Complete excision as determined by histologic examination of inked tissue margins was achieved in 88 of 91 (97%) surgeries, and 3 (3%) excisions were deemed incomplete. All incomplete excisions were of grade III FSAs. Tumor locations included interscapular or dorsal thoracic (n = 30), abdominal (22), parascapular (13), thoracic wall (15), and pelvic region or thigh (11). Thirty-five tumors were located on midline, 38 were to the right of midline, and 18 were to the left of midline.

Types of surgical procedures—Surgical techniques used for excision of ISS were summarized (Table 1). Ten cats were treated with a combination of surgical techniques because of tumor location and size. Of these, 1 cat had abdominal wall resection with ilial wing osteotomy, 4 had abdominal and chest wall resection, 2 had abdominal wall resection with dorsal spinous process osteotomies, 1 had a partial scapulectomy with dorsal spinous process osteotomies, and 2 had bilateral partial scapulectomies with dorsal spinous process osteotomies. Polypropylene mesh was used for reconstruction in 2 cats with lateral thoracic wall tumors; 1 of these cats also required reconstruction of the diaphragm and a partial liver lobectomy because of the extent of the tumor.

Outcomes—At the time of writing, 8 cats were still alive (follow-up range, 2,157 to 3,152 days) with no evidence of local tumor recurrence or metastasis. Thirty-two cats were lost to follow-up during the course of the study (follow-up range, 80 to 1,283 days), and 31 cats had died. Twenty-five cats died of non–tumor-related causes, and 26 died of suspected tumor-related causes. Local tumor recurrence was reported in 13 of 91 (14%) cats; for these cats, the median RFI was 309 days (IQR, 206 to 581 days; 95% CI, 161 to 457 days). Histologic analysis of ISS resected during definitive surgery in these 13 cats indicated that 1 was grade I, 2 were grade II, and 10 were grade III. Evidence of metastasis developed in 18 of 91 (20%) cats, and the median MFI for cats with evidence of metastasis was 309 days (IQR, 206 to 581 days; 95% CI, 161 to 457 days). Histologic analysis of ISS resected during definitive surgery in these 13 cats indicated that 1 was grade I, 2 were grade II, and 10 were grade III.

Table 1——Type and number (%) of surgical procedures performed in 91 cats that underwent radical excision (ie, tumor resection with 5-cm margins including 2 muscle planes or bone deep to the tumor) of ISS without adjunctive treatment and the number of cats in each group that had local tumor recurrence, had evidence of metastasis, or were lost to follow-up.

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>No. (%) performed</th>
<th>No. with local tumor recurrence</th>
<th>No. with metastasis</th>
<th>No. lost to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal wall resection</td>
<td>7 (8)</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Thoracic wall resection</td>
<td>2 (2)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Osteotomy of spinous processes</td>
<td>30 (33)</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Partial scapulectomy</td>
<td>3 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Osteotomy of ilial wing</td>
<td>1 (1)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hind limb amputation with hemipelvectomy</td>
<td>5 (5)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hind limb amputation with hip disarticulation</td>
<td>9 (9)</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Forelimb amputation with scapulectomy</td>
<td>7 (8)</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Soft tissue excision only</td>
<td>20 (22)</td>
<td>4</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Tail amputation</td>
<td>1 (1)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Combination of surgery types</td>
<td>10 (11)</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Calculations for percentage of cats that underwent the described surgical procedure were based on the total number of definitive surgeries performed (n = 91).
Twelve of 18 cats with metastasis had grade III FSAs, and 6 had grade II FSAs. No significant ($P = 0.967$) association was established between RFI and MFI. Four cats did have evidence of both recurrence and metastasis at the time of death. Sixteen cats had radiographic evidence of pulmonary metastasis, and 2 cats had metastasis to subcutaneous tissues; 1 of these 2 cats also had evidence of pulmonary metastasis. Of the 3 cats for which histologic evaluation indicated incomplete tumor excision, 1 cat had local tumor recurrence (RFI, 467 days) and was euthanized 524 days after definitive surgery. One cat was still alive 2,644 days after definitive surgery with no evidence of tumor recurrence, and the other was lost to follow-up but had no evidence of recurrence at last contact 1,283 days after definitive surgery. None of the cats received additional treatment for tumor recurrence or metastasis.

Median survival times were determined for all cats (Figure 1) and for cats that did or did not have local tumor recurrence (Figure 2) or evidence of metastasis (Figure 3). Overall median survival time was 901 days (IQR, 450 to 1,969 days; 95% CI, 317 to 1,485 days). Median survival time for cats with local tumor recurrence as calculated by means of Gehan-Breslow survival analysis was 499 days (IQR, 253 to 797 days; 95% CI, 199 to 264 days), whereas that for cats without metastasis was 1,292 days (IQR, 524 to 2,714 days). Evidence of tumor recurrence or metastasis had median survival times of 1,461 days (IQR, 569 to 2,371 days; 95% CI, 267 to 509 days). Cats with no evidence of tumor recurrence or metastasis had median survival time of 1,292 days (IQR, 524 to 2,714 days; 95% CI, 267 to 509 days). Cats with no evidence of tumor recurrence or metastasis had median survival times of 1,461 days (IQR, 569 to 2,371 days; 95% CI, 267 to 509 days). Only local tumor recurrence ($P = 0.002$) and evidence of metastasis ($P < 0.001$) were identified as independent predictors of survival ($\chi^2 = 59.18; P = 0.000$). The following variables were included in multivariate analysis: sex, time from tumor detection to definitive surgery, type of surgical procedure, maximum tumor diameter, recurrence, metastasis, cause of death, and tumor grade. The effect of type of surgery on survival time was also analyzed via several permutations, and no variation was considered significant (Table 2).

Complications—Major complications occurred in 10 of 91 (11%) cats; all were nonfatal. Seven cats had dehiscence of their surgical incisions that required a second surgical closure; all of these had interscapular tumors. The median maximum tumor diameter for interscapular tumors associated with dehiscence was 4 cm (IQR, 3.25 to 5.50 cm), and that for interscapular tumors not associated with dehiscence was 3 cm (IQR, 2.00 to 4.37 cm). No significant ($P = 0.966$) difference was detected between the sizes of interscapular tumors for which the surgical wound did (n = 7) or did not (23) dehisce. One cat developed laryngeal paralysis because of transection of the recurrent laryngeal nerve during soft tissue dissection. An arytenoid lateralization was performed with full recovery; the cat was doing well but was lost to follow-up at 547 days. One cat developed a chronic draining tract following the use of mesh for reconstruction of the thoracic wall; this cat was lost to follow-up at 212 days. One cat that underwent rib resection for a lateral thoracic wall tumor developed a pneumothorax and respiratory arrest immediately after definitive surgery. Thoracocentesis was performed, the thoracic wall defect was reconstructed, and the cat recovered successfully. Minor complications were recorded in 3 cats. Postoperative pneumonia was diagnosed in 1 cat and was treated successfully with antimicrobial drugs. Two cats had chronic constipation (1 after hemi-
pelvectomy and 1 after high tail amputation), and both were successfully managed with medical treatment.

Discussion

This report describes the use of radical surgery alone to treat ISS in cats. The surgical margins included 5 cm of tissue beyond the palpable edges of the tumor and 2 fascial planes or bone deep to the tumor. The primary objective of this retrospective study was to evaluate the impact of this radical excision on local recurrence and metastasis rates, survival times, and complications associated with surgery.

Radical surgery alone resulted in complete margins in 88 of 91 (97%) cases and a local tumor recurrence rate of 14%. Tumor recurrence significantly (P = 0.002) decreased median survival time. Previously reported overall rates of local tumor recurrence for ISS with surgery alone ranged from 35% to 59%15,21 and from 26% to 52% with adjuvant therapies, including pre- or postoperative radiation and chemotherapy.12-18,20,21 Other reports15,21 indicated that tumor recurrence affected survival time, although these data were not found to be significant in multivariate analysis in 1 study.21 Some studies revealed a significant decrease in tumor recurrence rates with complete (ie, tumor-free) surgical margins11,17 with chemotherapy,12 and without chemotherapy.20 Although some degree of caution should be used in comparison with historical controls because of variability among factors, the study described here detected lower tumor recurrence rates than those previously reported, regardless of the use of adjuvant therapies. Median RFI for the 13 cats in which tumors recurred was 309 days. Hershey et al22 reported a significant (P = 0.005) difference in RFI, with a median of 274 days for excision performed at a referral institution, compared with 66 days for surgery performed by a referring veterinarian, stating that referring veterinarians were more likely to perform marginal excision.22 The same study found that a combined group of cats treated with wide (≥3 cm) or radical (amputation) excision had a significantly higher RFI than did those treated with marginal excision (<3 cm). In another report,14 the median RFI for cats after surgery plus postoperative radiation had not been reached at the conclusion of the study, whereas for cats treated with surgery, postoperative radiation, and chemotherapy, the median RFI was 661 days. Although it may appear that adjuvant treatment increases RFI, the scope of the study reported here was to evaluate the effects of radical surgery without the influence of adjuvant treatment. Further evaluation of radical surgical treatment of ISS, in conjunction with radiation or chemotherapy, would be necessary to determine whether RFI can be increased for cats treated via this method with the addition of adjuvant treatment.

Previously reported median survival times and local tumor recurrence rates in cats during or after various treatments for ISS reflect the need for a more aggressive treatment. With surgery alone, median survival time has been reported as >395 days,12 576 days22 and 804 days21. In addition, Romanelli et al21 reported a lower median survival time of 707 days after surgery plus adjuvant treatment, compared with surgery alone. Other studies13-15,20 in which investigators evaluated pre- or postoperative radiation in addition to surgical excision reported similar survival times, ranging from 600 to 842 days13-15,20. Recently, Eckstein et al reported a 1,300-day median survival time for cats after surgery and postsurgical radiation with curative intent. Thirty-three percent of those cats received adjuvant treatments after disease progression was documented, although this was not shown to affect survival.31 In the study reported here, radical surgical excision resulted in an overall median survival time of 901 days; however, the median survival time was greater for cats without tumor recurrence or evidence of metastasis (1,461 and 1,528 days, respectively).

The overall metastasis rate in cats of the present study was 20% (18/91 cats), with metastasis significantly (P < 0.001) affecting overall survival. Rates of metastasis of ISS have been reported to range from 5.6% to 22.5%,15-17,21,22 and metastatic disease has been shown to significantly decrease survival time in cats.6,13,21 Pulmonary metastasis is most commonly reported; metastasis to other sites, in-

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Median survival time (d)</th>
<th>95% CI (d)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparison 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue only</td>
<td>901</td>
<td>≤241 – 2,043</td>
<td>0.556</td>
</tr>
<tr>
<td>Dorsal spinous processes</td>
<td>820</td>
<td>246 – 1,394</td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>797</td>
<td>−368 – 1,962</td>
<td></td>
</tr>
<tr>
<td>Comparison 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue only</td>
<td>901</td>
<td>≤241 – 2,043</td>
<td>0.376</td>
</tr>
<tr>
<td>Soft tissue and bone</td>
<td>878</td>
<td>434 – 1,321</td>
<td></td>
</tr>
<tr>
<td>Comparison 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue only</td>
<td>901</td>
<td>≤241 – 2,043</td>
<td>0.746</td>
</tr>
<tr>
<td>Axial skeleton</td>
<td>1,039</td>
<td>405 – 1,673</td>
<td></td>
</tr>
<tr>
<td>Appendicular skeleton</td>
<td>797</td>
<td>−769 – 2,363</td>
<td></td>
</tr>
</tbody>
</table>

Types of surgery evaluated in various comparisons were not significantly associated with survival time.
including regional lymph nodes, skin, intestine, spleen, epi-
dural and ocular infiltration, and multiorgan involvement
has also been reported.10,22,32,33 Although investigators in
1 study reported a 5.6% metastasis rate in cats treated
with surgery and chemotherapy, other studies14,15,18,20 that
also evaluated chemotherapeutic protocols as adjuvant
treatment after surgery for ISS have not conclusively sup-
ported the effectiveness of chemotherapy in reducing rates
of metastasis. Rates of metastasis in the present study were
comparsion between that study and the present study
were analyzed via several permutations, and these
results indicated that the type of surgery did not influ-
ence outcome.

Compared with non-ISS, ISS induce a greater in-
flammatory response, characterized histologically by a
predominately lymphocytic infiltration, along with in-
creased cellular necrosis, increased mitotic rates, and
the presence of multinucleated giant cells.10,36,37 Results
of a recent study indicated that ISS were associated
with higher histologic grades than were non-ISS, but
no discussion of prognosis was provided. Various stud-
ies have found a low prevalence of high-grade (ie, grade
III) ISS in cats, whereas these had a high prevan
nance as a component of grade III tumors, compared with grade I or II
tumors, and grade was not significantly associated with
survival times. High tumor grades in humans with soft
tissue sarcomas have been correlated with metastasis
rates and survival times but not with local recurrence.28
In dogs with soft tissue sarcomas, tumor grade was sig-
nificantly associated with likelihood of metastasis,
whereas the only prognostic indicator for local tumor
control was complete surgical removal.30 In the present
study, grading of ISS was performed as previously de-
scribed for soft tissue sarcomas in various species,13,26,30,36
and for sarcomas, grade is considered more important
than the cell of origin.29 Grade assessment can be sub-
jective, although schemes similar to that described for
soft tissue sarcomas that include calculation of a mitot-
ic index and a percentage of tumor necrosis appear to
be reproducible.32 To minimize variability in the analy-
sis of feline ISS in the present study, tissues were his-
tologically evaluated by 1 pathologist (BEP) who had
reviewed prognostic factors for soft tissue sarcomas in
dogs.32 Variations in the methods of earlier studies of
ISS in cats make comparison difficult, as it cannot be
assumed that tumor grade classification among studies
is consistent.

One of the greatest concerns regarding radical
excision of soft tissue tumors is the nature and inci-
dence of surgical complications, most notably wound
dehiscence caused by excessive tension. We report here
a major complication rate of 11% (10/91 cats), with
wound dehiscence being the most commonly encoun-
tered problem; none of these complications was fatal.
This appears to compare favorably with previously re-
ported rates of 15% for nonfatal complications associat-
ed with aggressive surgical resection of ISS,30 although
comparison between that study and the present study

To the authors’ knowledge, there are no current
reports aside from the present study that evaluate con-
sistently performed radical surgery in cats for the
treatment of ISS. Investigators of several stud-
ies inconsistently used wide or radical ex-
cision methods or excised tissues 1 fascial plane or
muscle layer deep to the tumor, resulting in complete
surgical margins on histologic examination in 46% to
80% of cases. Wide, complete surgical margins were
achieved in 88 of 91 (97%) cases in the present study.
A recent report described achievement of complete
surgical margins in 95% of cases; excision was per-
fomed by 1 surgeon using 4- to 5-cm lateral margins
including tissues 1 fascial plane deep to the tumor,
with osteotomies of spinous processes, partial scapu-
lectomy, and amputation where indicated. Addition-
ally, investigators in 1 study reported complete sur-
gical margins for 75% of appendicular tumors treated
with amputation, compared with incomplete margins
for 100% of tumors treated with wide local exci-
sion. Several studies have correlated complete
surgical margins with increased survival times and
disease-free intervals. Completeness of surgical mar-
gins was not identified to have prognostic value in
the study reported here; however, there were only 3
cases in which complete margins were not achieved,
suggesting that more aggressive surgery may be war-
ranted to attain complete margins and effectively de-
crease rates of recurrence and increase survival time
in cats with ISS.

Injection-site sarcomas are poorly circumscribed,
are not encapsulated, and are more locally invasive
than their non–vaccine-associated counterparts.10 In
humans, soft tissue sarcomas often lie in contact with
but rarely invade cortical bone.34 Likewise, interscap-
ular ISS in cats are thought to extend to, but not to
invade, spinous processes of the vertebral column.35

There is no evidence in the current literature suggesting
that feline ISS are associated with bone involvement;
however, complete surgical excision is difficult because
of the rapid growth, lack of encapsulation, and exten-
sive microscopic invasion of tumor cells.36 Although
not involving bone, locally invasive ISS can extend to
the soft tissue–bone interface, necessitating removal of
the underlying bone as a deep surgical margin during
radical excision. Although investigators in 1 study re-
ported a significantly (P = 0.04) shorter initial time to
first event (defined as tumor recurrence, metastasis, or
death) with removal of bone, this variable was not sig-
nificantly associated with overall time to first event.
Removal of bone was not correlated with a negative effect
on outcome in other studies.39,41 In the study reported
here, 32 of 91 cats underwent osteotomies of spinous
processes, hemipelvectomy, amputation, rib resection,
partial scapulectomy, and ilial wing ostectomy as part
of the radical excision of ISS. The various types of sur-
gery were analyzed via several permutations, and these
results indicated that the type of surgery did not influ-
ence outcome.

The presence of multinucleated giant cells.
These have been reported rates of 15% for nonfatal complications associat-
ed with aggressive surgical resection of ISS, although
comparison between that study and the present study

11–13,16,18,19
is difficult. However, all major complications were successfully treated with a second surgery. The wound dehiscences that occurred in cats of the study reported here were associated with the excision of interscapular tumors and were successfully treated with mechanical debridement and an additional surgery for secondary closure. Incisional dehiscence was likely due to a combination of increased wound tension and high motion of the wound bed, although subjectively, excessive tension was not observed in the immediate postoperative period for any interscapular tumor excision. Owners were instructed at the time of discharge to strictly enforce patient confinement until the time of suture removal. It was difficult in a retrospective study that encompassed a 10-year period to identify the differences between the 23% of 30 interscapular incision sites that dehisced and the 77% of interscapular wounds of similar size and nature that did not dehisce. It is possible that additional factors, such as lack of exercise restriction by owners, increased motion that resulted in undue tension on the wound, and possible patient factors, including underlying disease or debilitation, may have caused dehiscence.

Perioperative surgical complications were recorded for several cats. Pneumothorax developed in 1 cat because of incomplete closure of the thoracic wall defect, which was immediately corrected with no detrimental effects. Transection of the left recurrent laryngeal nerve occurred during excision of a cervically located tumor. Although medical management is often recommended for unilateral laryngeal paralysis in cats,38 surgical treatment of this iatrogenic case was performed. Arytenoid lateralization in cats has been associated with low rates of complications, with failure of the initial surgical repair reported as the most common complication.38 The cat that underwent the procedure in the present study was lost to follow-up 18 months after surgery but did not have evidence of any respiratory or musculoskeletal complications at that time. Two cats were reported to have mild chronic constipation, 1 following a proximal coccycgeal amputation and 1 following hemipectectomy; both were treated medically with dietary fiber and laxatives. It is possible that a neurogenic (sacral nerve) etiology or loss of a stable pelvic diaphragm may have caused constipation in these 2 cats. Another complication was the development of chronic draining tracts over incompletely resected tumors. To prevent dehiscence, incisional inflammation may not have been documented and, because of the retrospective nature of this study, could not be retrieved. This is a limitation that may have falsely lowered the complication rate.

Another limitation of the present study was the lack of preoperative imaging by use of CT or MRI for surgical planning. During the study period, MRI equipment was not readily available. Conventional single-slice CT was accessible but, because of time and financial constraints perceived by the primary surgeon, was not employed in the surgical planning process. It was also the surgeon’s impression that the extent of the tumor was palpable during physical examination, and with an excision that included 5-cm surgical margins, it was thought the tumor would not invade the planned margins. However, in 1 study,42 use of CT resulted in reclassification of 17 of 26 subcutaneous neoplasms in dogs to a more advanced clinical stage, compared with that determined via physical examination. Investigators in 1 recent study12 used CT in all cases for surgical planning, and the resulting recurrence rates were similar to those described in other studies.5,13,16,19,21 The authors of the present study are not aware of any other study of feline ISS in which CT was consistently used for preoperative surgical planning; CT was performed for preoperative assessment2,5,21,32 or was used for preoperative radiation planning13,16 in some, but not all, cats in other studies. With helical CT and MRI becoming more readily available in veterinary medicine, the authors recommend that presurgical planning with advanced imaging techniques be consistently performed. It should also be considered that, given the aggressive nature of ISS, physical examination may result in underestimation of tumor size. Without the use of CT or MRI for surgical planning, the use of 5-cm margins in the study reported here may have increased the likelihood of complete excision of the tumor, resulting in decreased recurrence rates. Further investigation would be necessary to determine whether the addition of advanced imaging for tumor staging has any effect on the completeness of surgical excision, rates of recurrence, and survival time in the treatment of ISS.

Other limitations, defined by the retrospective nature of the present study, may have falsely lowered the rates of local tumor recurrence and metastasis. Twenty-one cats received either pre- or postoperative radiation treatment. The authors attempted to delineate the data and included only cats treated with radical surgical excision; the exclusion of cats that underwent preoperative radiation treatment for large tumors which may have precluded complete excision and of cats that had incomplete tumor excisions in which postoperative radiation treatment was performed may have introduced bias into this study. Additionally, necropsies were not performed to determine causes of death, and follow-up with thoracic radiography was not reliably performed. These factors may also have resulted in lower reported rates of tumor-related deaths. Conversely, our rate of recurrence or metastasis may have been erroneously increased, as most were not histologically confirmed and may have represented other pathological processes. Thus, it must be considered that although every attempt to report accurate data was made, some degree of bias is likely to exist in a retrospective study of this sample size.

Another weakness of the study was the large number of cats lost to follow-up. An argument could be made
to use a time-to-failure model, which would assume that all data have met the study criteria and therefore would not be censored. To test this hypothesis, we performed an analysis in which all data were assumed to have met the study criteria (and subsequently were not censored), which resulted in a median survival time of 547 days (IQR, 294 to 1,283 days). However, this analysis seriously underestimates the contribution that cats that were still alive at the end of the study would have on survival times. This conclusion was confirmed via an analysis in which we excluded all the cases that were lost to follow-up (n = 32) but censored the cats that were still alive at the end of the study (8) and found a median survival time of 701 days (IQR, 259 to 1,797 days). In addition, the cats that were censored as lost to follow-up had a median survival time of 462 days (IQR, 323 to 584 days), which was longer than the median time to evidence of metastasis. Additionally, the Gehan-Breslow statistic was chosen because it is more conservative than the log-rank test for survival analysis. Another reason for this choice was that the censored data are assumed to be less accurate with the Gehan-Breslow statistic, and censored data are given less weight to reduce the influence on the later survival times.

Radical excision of feline ISS with 5-cm margins including 2 muscle planes or bone deep to the palpable tumor resulted in acceptable complication rates despite large surgical resections. Further evaluation of adjuvant treatment in addition to the proposed surgical treatment is warranted but was beyond the scope of this study. Radical excision of ISS resulted in a similar rate of metastasis, compared with previous reports. However, our reported recurrence rate appears to be substantially less than rates reported with less aggressive surgeries, with or without adjuvant treatment, suggesting that radical excision may be a valuable means of attaining an improved outcome in the treatment of ISS in cats.

References


a. PromAce (acepromazine maleate) injection, 10 mg/mL, Fort Dodge Animal Health, Overland Park, Kan.
b. Robinul (glycopyrrolate) injection, 0.2 mg/mL, Baxter Healthcare Corp, Deerfield, Ill.
c. Morphine sulfate injection, 15 mg/mL, Baxter Healthcare Corp, Deerfield, Ill.
d. PropOFlo, 10 mg/mL, Abbott Laboratories, Abbott Park, Ill.
e. Isofo, Abbott Laboratories, Abbott Park, Ill.
f. Sharpie, Sanford Brands, Oak Brook, Ill.
g. Surgipro polypropylene mesh, United States Surgical Corp, Norwalk, Conn.
h. PDS II (polydioxanone) suture, Ethicon Inc, Somerville, NJ.
i. Appose ULC Skin Stapler 35W, United States Surgical Corp, Norwalk, Conn.
j. Ethilon nylon suture, Ethicon Inc, Somerville, NJ.
k. Duramorph morphine sulfate for injection (preservative free), 1 mg/mL, Baxter Healthcare Corp, Deerfield, Ill.
l. Lidocaine HCl for injection (preservative free) 2%, APP Pharmaceuticals, Schaumburg, Ill.
m. Marcaine (bupivacaine hydrochloride 0.25%), AstraZeneca Pharmaceuticals LP, Wilmington, Del.
n. Fentanyl citrate injection, 50 µg/mL, Baxter Healthcare Corp, Deerfield, Ill.
o. Duragesic-25 fentanyl, 2.5 mg (10 cm2) transdermal patch, Janssen Pharmaceuticals Inc, Titusville, NJ.
p. Codine phosphate oral solution, 15 mg/5 mL, Roxane Laboratories Inc, Columbus, Ohio.
q. Narcan naloxone HCl, 1 mg/mL, Dupont Pharmaceutical Co, Wilmington, Del.
r. SigmaPlot for Windows, version 11.00, Systat Software Inc, Chicago, Ill.
s. Statistica, version 6, StatSoft Inc, Tulsa, Okla.


