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# Marginal resection and adjuvant strontium plesiotherapy in the management of feline eyelid malignant peripheral nerve sheath tumours: two cases

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## Abstract

**Case series summary** Two cats with a marginally resected eyelid malignant peripheral nerve sheath tumour were treated with adjuvant strontium plesiotherapy a few weeks after surgery. The dose applied in both cases was 200 Gy to the surface, in five fractions, on a Monday–Wednesday–Friday basis. The treatment aimed to achieve a clinical margin of approximately 1 cm around the surgical scar and multiple application fields were required to cover such an area. Local recurrence was not seen in either case after 1330 and 645 days, respectively.

**Relevance and novel information** The majority of periocular malignant peripheral nerve sheath tumours reported in the literature recur after surgery. In the two cases described in this report the combination of surgery and adjuvant plesiotherapy has been able to provide good local control with minimal toxicity. This multimodal approach could be considered as an alternative to aggressive surgery such as enucleation or exenteration.

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## Introduction

In people, peripheral nerve sheath tumours (PNSTs) are a group of neoplasms that arise from Schwann cells, perineurial cells and intraneuronal fibroblasts. Depending on their cell of origin, PNSTs can be further divided into schwannoma, neurofibroma and malignant PNSTs, respectively. According to the most recent edition of the World Health Organization's International Classification of Tumors of Domestic Animals, PNSTs are, in veterinary medicine, divided into only benign and malignant variants because of their uncertain histogenesis.<sup>1</sup> PNSTs can be difficult to differentiate histologically from other spindle-cell tumours such as perivascular wall tumours and fibrosarcomas, and immunohistochemistry is often required to substantiate the diagnosis. The most common immunohistochemical marker used to support the morphological diagnosis of PNSTs is S100, which is expressed in up to 100% of cases.<sup>2</sup>

A recent retrospective study described pathological and clinical characteristics of 59 PNSTs in 53 cats.<sup>2</sup> There were 43 benign PNSTs and 16 malignant PNSTs. The overall recurrence rate in the study was 23% (13/57).

The recurrence rate for benign PNSTs was 15% (6/41); none of the tumours removed with clear margins recurred (19/19), while recurrence was seen in 27% (6/22) of the incompletely removed tumours. Between benign PNSTs, only one involved the lower eyelid and the tumour recurred after incomplete excision; another three were completely removed from the periocular skin, and none of them

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recurred. The recurrence rate of malignant PNSTs was 44% (7/16); none of the tumours removed with clear margins recurred (6/6), while recurrence was seen in 70% (7/10) of the tumours removed with incomplete margin. Of the malignant PNSTs there was one tumour involving the upper eyelid and the tumour recurred after incomplete excision.

In another recent retrospective series describing 43 feline eyelid tumours submitted to a single pathology laboratory, there were three PNSTs involving the eyelid.<sup>3</sup> In this study PNSTs were not classified as benign or malignant and margins of excision were not reported. All three eyelid PNSTs recurred after surgical excision.

A recent case series described presentation and outcome of cutaneous periocular PNSTs in six cats.<sup>4</sup> As in the previous study, PNSTs were not divided into benign and malignant and margin of excision were not described. All six tumours recurred, on average, three times after conservative surgical excision. After multiple conservative surgeries, four of these cats underwent exenteration or enucleation as a curative-intent procedure; none of the cats undergoing aggressive surgery presented tumour recurrence.

Radical or wide surgical resection or debulking surgery followed by adjuvant radiotherapy is considered the treatment of choice for the management of soft tissue sarcomas in cats and dogs.<sup>5</sup> However, adjuvant irradiation of the periocular area with external beam radiotherapy using curative-intent doses (>45 Gy) is limited by the risk of incurring in severe toxicity. Side effects reported in this location include dermatitis, conjunctivitis, keratitis, iritis or chronic complications such as chronic keratoconjunctivitis sicca, corneal ulceration, secondary uveitis, chronic conjunctivitis, cataract formation, radiation retinopathy and optic neuropathy.<sup>6-9</sup>

Strontium plesiotherapy consists of the direct application of the radioactive source to the tumour surface. Strontium 90 undergoes beta ( $\beta$ )-decay emitting  $\beta$ -particles, which are characterized by limited penetration ability into the irradiated tissue (2–3 mm). The shallow penetration is the main attraction of this treatment because it allows applying a large dose of radiation to the surface without affecting the deeper tissue. Strontium plesiotherapy has been successfully used in the treatment of various periocular tumours in cats and dogs; for example, feline mast cell tumours,<sup>10,11</sup> canine limbal melanoma<sup>12</sup> and canine limbal hemangiosarcomas.<sup>13</sup>

Herein, we present the use of conservative surgery followed by adjuvant strontium plesiotherapy in the treatment of two cases of malignant feline PNSTs involving the eyelid. Histopathology and immunohistochemistry in both cases were reviewed by a board-certified pathologist (RR).

## Case series description

### Case 1

A 11-year-old, female, neutered, domestic longhair cat was presented to the Ophthalmology Unit with a 4 mm

mass on the left lower eyelid (Figure 1a). Cytology showed a spindle cell neoplastic population with severe nuclear atypia and occasional multinucleated cells. Staging including thoracic radiographs and abdominal ultrasound showed no evidence of metastatic disease.

Treatment options, including aggressive surgery or more conservative surgery followed by strontium plesiotherapy, were discussed with the owners and they elected for the more conservative approach. A wedge resection of the mass with double layer closure was performed, leaving a relatively tight lower eyelid (Figure 1b), but no functional problems.

Histology revealed a poorly demarcated neoplastic proliferation of spindle cells expanding the eyelid dermis and arranged in bundles with occasional nuclear palisading. These cells displayed moderate anisocytosis and marked anisokaryosis. Multinucleation was occasionally evident. Mitoses were 10 in 10 high-powered fields (HPFs). A histological diagnosis of soft tissue sarcoma, most likely a malignant PNST, was made. Immunohistochemistry showed that the neoplastic cells were positive for S100, confirming the diagnosis of malignant PNST. The margin of excision was narrow (2 mm).

Strontium plesiotherapy was started 20 days after surgery. The treatment was delivered on a Monday–Wednesday–Friday basis for five fractions to a total surface dose of 200 Gy. Each fraction consisted of five contiguous application fields to obtain a clinical margin of approximately 1 cm around the scar. The globe was protected from the radiation field using a Jaeger lid plate. No acute side effects developed during the treatment and the cat was discharged without any medication.

At re-examination 5 weeks later the owner reported no side effect apart from radiation-induced localized alopecia (Figure 1c). The left eye was comfortable, with no evidence of ophthalmic abnormalities. Eyelid function and tear production were normal. Alopecia was still present at the second re-examination 6 months later, but the remainder of the ophthalmological examination was unremarkable.

After collapsing, the cat was presented to the referring vet after 1330 days and the owner elected for euthanasia without any further investigations. At the time of the consultation there was no evidence of local recurrence. The owner did not allow a post-mortem examination.

### Case 2

A 5-year-old, female, neutered, domestic shorthair cat was referred to the Oncology Unit after incomplete excision of a 7 mm mass from the lateral aspect of the left lower eyelid. A blepharoplasty had been performed to resect the mass, but information about the specific surgical technique used was not available upon referral.

Histology revealed a poorly demarcated spindle cell proliferation expanding the eyelid dermis with cells organized in bundles and admixed with oedematous



**Figure 1** Case 1: malignant peripheral nerve sheath tumour of the left lower eyelid (a) before and (b) after surgery. (c) Alopecia 5 weeks after the end of strontium plesiotherapy. Case 2: (d) plastic Jaeger lid plate in place to protect the eye during strontium plesiotherapy. (e) Cutaneous acute moist dermatitis 2 weeks after treatment, (f) followed by leukotrichia after a few months.

fibrillar matrix. Anisocytosis and anisokaryosis were moderate and mitoses were 2 in 10 HPFs. Small areas of necrosis were noted scattered throughout the tumour. The tumour was initially diagnosed as incompletely excised soft tissue sarcoma and subsequent immunostaining for S-100 allowed a final diagnosis of malignant PNST.

Revision surgery using a more aggressive approach or adjuvant plesiotherapy was discussed with the

owners, and they elected for the more conservative approach.

Strontium plesiotherapy was started 33 days after surgery. The treatment was delivered on a Monday–Wednesday–Friday basis for five fractions to a total surface dose of 200 Gy. Each fraction consisted of six contiguous application fields providing a clinical margin of approximately 1 cm around the scar. During the treatment the globe was protected using a plastic Jaeger lid

plate (Figure 1d). At the end of the radiation course there was mild erythema in the irradiated area. Meloxicam was prescribed for 3 weeks as an anti-inflammatory and analgesic. A few days after the end of the radiotherapy moist desquamation developed (Veterinary Radiation Therapy Oncology Group grade 2 skin acute toxicity;<sup>9</sup> Figure 1e).

At re-examination 3 weeks later, the dermatitis was completely resolved, but the irradiated area was completely alopecic. At re-examination after 6 months, the irradiated area presented diffuse leukotrichia (Figure 1f), but there was no evidence of chronic ocular toxicity.

At the time of writing, 645 days after the end of the radiotherapy, the cat is still well and there is no evidence of tumour recurrence.

## Discussion

Marginal resection followed by strontium plesiotherapy was able to provide good local control in the two cases presented herein without performing aggressive surgery such as enucleation or exenteration. This was an extremely promising result considering that 11/14 periocular PNSTs reported in the literature recurred after surgical excision.<sup>2-4</sup>

The dose of radiation prescribed in these two cases was 200 Gy to the surface or 50 Gy at a depth of 2 mm,<sup>14</sup> which is comparable with the total dose commonly prescribed as adjuvant treatment in cats with injection-site sarcoma treated with external beam radiotherapy.<sup>15</sup>

Compared with external beam radiotherapy, strontium plesiotherapy can be used to treat small areas (2–8 cm<sup>2</sup>) because only a limited number of contiguous fields can be successfully applied to an area. Both tumours presented in this report underwent surgery when their size was still small (4 and 7 mm, respectively), leaving a surgical scar smaller than 1 cm. A margin of approximately 1 cm around the scar was applied to define the treatment area, but this decision was driven by the practicality of the treatment, as specific data are not available in the literature. When planning external beam radiotherapy as adjuvant treatment of injection-site sarcomas a margin of 3 cm around the surgical scar is commonly applied because of their tendency to infiltrate along the fascial planes.<sup>15,16</sup> In the two cases presented in this series, we applied a narrower margin because non-injection site sarcomas are less biologically aggressive and infiltrative than injection-site sarcomas.<sup>17</sup>

Acute and long-term side effects associated with the treatment were limited to the skin and very mild. At re-examination at 6 months there was no evidence of ocular toxicity such as cataract. In this sense we think that protecting the eye with a plastic Jaeger lid plate provided further attenuation to the already weak deep radiation dose.

## Conclusions

Excisional globe-sparing surgery of small periocular PNSTs followed by adjuvant plesiotherapy may be a valid alternative to enucleation or exenteration. A larger number of cases would be necessary to further support the positive outcome seen in these cases.

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