Peripheral nerve tumors may be of neuroectodermal origin, derived from the neural sheath, or of non-neural sheath origin. Benign peripheral nerve sheath tumors (BPNSTs) include neurofibromas and schwannomas, which collectively constitute 10%-12% of benign soft-tissue neoplasms.\(^{19,28,29}\) Malignant PNSTs (MPNSTs) represent 5%-10% of all soft-tissue sarcomas and occur in 0.001% of the general population.\(^{12,30}\)

Both BPNSTs and MPNSTs may occur sporadically, or in association with autosomal dominant neurofibromatoses (NFs). Sixty percent of patients with neurofibromatosis Type 1 (NF1)—the most common NF—will develop solitary, diffuse, or plexiform benign neurofibromas, the latter two occurring almost exclusively in patients with NF1.\(^{11,26}\) NF1-associated neurofibromas have an estimated 10%-15% risk of malignant transformation, with internal plexiform tumors at the highest risk of conversion.\(^{32}\) MPNSTs occur in up to 10% of NF1 patients over their lifetimes; conversely, half of all MPNSTs are seen in NF1 patients.\(^5\)

Peripheral schwannomas are typically sporadic, although...
up to 10% are associated with NF Type 2 (NF2). Rarely, patients may present with schwannomatosis, a largely sporadic disorder that is predisposed to nonvestibular nonintradermal schwannomas. 

Surgical excision remains the primary treatment modality for BPNSTs. Similar techniques are used for intraneural schwannomas, which arise from a single fascicle, and neurofibromas, which often have multiple thicker fascicles entering and exiting the tumor capsule. MPNSTs are treated best with wide surgical margins, followed by chemotherapy and local radiation; unfortunately, metastases are common, with poor long-term survival.

Here, we present a series of 201 benign and malignant PNSTs treated surgically over 17 years at Toronto Western Hospital. This represents one of the largest surgical series of PNSTs in the literature, which was collected over a relatively short period and predominantly treated by a single surgeon (A.G.) at a multidisciplinary institution with electrophysiologists, neurologists, and radiation and medical oncologists. The aim of the study is to identify predictors of neurological deficit, tumor recurrence, and extent of resection using multivariate analyses, as well as the impact of genetic predisposition syndromes on tumor location and frequency.

Methods

The charts of all patients with PNSTs who were treated surgically at the Division of Neurosurgery at Toronto Western Hospital between 1993 and 2010 were reviewed retrospectively. One hundred seventy-five patients with 201 primary tumors had adequate follow-up data for analysis. The mean follow-up time for all patients was 29.5 months. Institutional research ethics board approval was obtained from the University Health Network.

Preoperative Workup

All patients had their full medical histories evaluated (including family histories) and underwent general physical and neurological examinations, as well as screening for the signs of NF. Patients with the clinical findings of NF1 or NF2 were referred to a multidisciplinary NF clinic for screening neuroimaging, genetic testing, and counseling. MRI was performed on all cases. In patients with benign-appearing lesions on imaging, excisional biopsy was typically recommended for symptomatic lesions, lesions with interval growth during follow-up, or any lesions in NF1 patients that changed in size. In patients with suspected malignancy, which was often based on rapid clinical growth, irregular margins, and/or heterogeneous gadolinium enhancement on MR imaging, a preoperative needle or open biopsy was sometimes performed or intraoperative pathology was obtained to determine the need for wide excision.

Surgical Technique

Intraoperative nerve stimulation with electromyography recording was used in all procedures. Surgery for BPNSTs was performed according to established microsurgical principles. For schwannomas, fascicles adherent to the capsule were bluntly dissected off. One or sometimes 2 fascicles were typically seen entering and leaving the tumor, and these were sectioned following electrophysiological confirmation of a lack of motor activity. The tumor was then removed en bloc. Larger tumors were enucleated via intracapsular dissection, followed by removal of the capsule if it was not densely adherent to the surrounding fascicles. Neurofibromas typically had 2 or more entering and exiting fascicles and required more careful dissection, but with the same principles as for schwannoma resection.

Surgical management of MPNSTs generally involved local excision with wide margins. Amputation was performed in 1 case, following intraoperative histological confirmation of the malignancy with negative preoperative workup for systemic metastases.

Data Collection

The impact of sex, age, NF diagnosis, tumor location, tumor size, and extent of resection on the recurrence of PNSTs was explored. Along with these parameters, the impact of preoperative motor or sensory deficits or neuropathic pain on the patients’ respective postoperative outcomes was assessed. Tumor location was categorized as either the extremity (upper or lower) or paraspinal plexus (brachial, thoracic, or lumbosacral). Preoperative tumor size was volumetrically approximated as a cylinder based on the maximal in-plane dimensions. The extent of resection was classified as gross-total (GTR) resection or subtotal resection (STR) based on the intraoperative findings. For BPNSTs, GTR implied complete removal of the tumor capsule and parent fascicles; for MPNSTs, GTR was signified by negative surgical margins on frozen section and permanent pathology. Neuropathic pain was identified based on the patient reporting lancinating or dysesthetic pain in an identifiable nerve distribution. Postoperative motor/sensory/neuropathic pain scores were dichotomized as either stable/improved or worse relative to the preoperative status based on objective confrontational testing of motor function and patient self-reporting of sensory function and neuropathic pain.

All patients were followed up at 4–6 weeks for incision inspection and the first follow-up gadolinium-enhanced MRI at 3 months. The frequency of the subsequent MRI studies was variable, depending on the extent of resection and NF status. Tumor recurrence was defined as evidence of a new contrast-enhancing lesion on postoperative T1-weighted MR images.

Statistical Analysis

Statistical comparison of the continuous variables was performed using the Student t-test; categorical variables were compared using the chi-square or Fisher’s exact tests, as appropriate. Multiple logistic regression models were used to identify predictors of tumor recurrence, worsened postoperative motor/sensory/pain outcomes, as well as STR, with appropriate odds ratios and confidence intervals computed for each. Explanatory variables were incorporated into the model with forward stepwise progression; nonsignificant interaction terms were dropped to create the final models. The significance levels for all tests were
set at $p < 0.05$. All statistical analyses were conducted using SPSS version 21 (IBM Corp.).

**Results**

**Patient and Tumor Characteristics**

In our cohort of 175 patients, the mean age at presentation was 45.2 years, and the patients with neurofibroma or MPNST were younger than the patients with schwannoma ($p < 0.001$). In total, 54.9% of patients were male, with no difference in the sex distribution across tumor histopathologies (Table 1). Of the 201 tumors in our cohort, there were 49 neurofibromas, 133 schwannomas, and 19 MPNSTs. Twenty-six of the 49 neurofibromas were associated with NF1, and 21 schwannomas were associated with NF Type 3 (NF3) (Table 2). Sixteen of 19 MPNSTs in our series were in patients diagnosed with NF1. The tumor size at diagnosis was available for 57 schwannomas and 20 neurofibromas in our series, with average sizes of $3.86 \times 4.89 \times 3.54$ cm and $4.12 \times 6.00 \times 3.98$ cm, respectively (Table 1). The difference in the volumetric preoperative size between schwannomas and neurofibromas was not statistically significant ($p = 0.336$).

The anatomical locations of all benign tumors in our cohort are shown in Table 2. Schwannomas were found most commonly in the brachial plexus, lower extremity, and lumbosacral plexus. Neurofibromas showed a similar localization, but with significantly fewer tumors located in the upper extremity. Twelve of the 49 neurofibromas in our series were plexiform. Four of the 19 MPNSTs were in the brachial plexus, lower extremity, and lumbosacral plexus. Neurofibromas showed a similar distribution relevant to their resected PNST (OR 29.55; 95% CI 1.24–702.69; $p = 0.028$); this association did not reach statistical significance for the entire cohort. In the univariate analyses, among BPNSNs, GTR (OR 0.22, 95% CI 0.078–0.60; $p = 0.002$) was significantly less likely to be achieved for MPNSTs than BPNSNs (OR 0.25, 95% CI 0.12–0.50; $p < 0.001$). This difference persisted when plexiform neurofibromas were excluded; GTR was achieved for 51.4% of nonplexiform neurofibromas. Tumor location influenced the extent of resection specifically for schwannomas but not neurofibromas; schwannomas located in an extremity were more likely to be fully resected than plexal tumors (brachial/thoracic/lumbosacral) (OR 3.36, 95% CI 1.41–8.00; $p = 0.007$), and schwannomas in the brachial plexus were more likely to be fully resected than those in the lumbosacral plexus (OR 4.76, 95% CI 1.39–7.87; $p = 0.01$). NF status did not influence the extent of resection for any BPNSNs. GTR was significantly less likely to be achieved for MPNSTs than BPNSNs (OR 0.22, 95% CI 0.078–0.60; $p = 0.002$); limb-sparing surgery was performed in all but 1 patient with MPNST in our series.

**Motor, Sensory, and Pain Outcomes**

The symptomatic presentation of all 201 tumors in our series is summarized in Table 3. In total, 12.8% of cases of schwannoma, 30.6% of cases of neurofibroma, and 36.8% of cases of MPNST presented with a preoperative motor deficits attributable to their PNST. Of these, all patients with schwannomas or neurofibromas remained stable or improved postoperatively, with permanent worsening seen in 2 of 7 MPNST patients (Fig. 1). New motor deficits were seen in 12 schwannoma patients (6 permanent) and 4 neurofibroma patients (3 permanent). Among the patients with a preoperative motor deficit, a diagnosis of MPNST was associated with an increased likelihood of worsened postoperative motor function relative to a diagnosis of BPNST (OR 4.01, 95% CI 1.21–13.22; $p = 0.023$) and the presence of a preoperative motor deficit (OR 8.06, 95% CI 4.65–17.59; $p = 0.038$) were associated with an increased likelihood of stable/improved postoperative motor function. Only GTR was an independent predictor of stable/improved postoperative motor function in the multivariate analysis. Age, sex, tumor histopathology, NF status, location and tumor size were not significant predictors of postoperative motor outcome.

In total, 30.1% of patients with schwannomas, 44.9% of patients with neurofibromas, and 26.3% of patients with MPNSTs presented with paresthesia or numbness in a distribution relevant to their resected PNST. In total, 59.2% had a positive Tinel’s sign in the relevant nerve distribution. Postoperatively, the worsening of preexisting sensory disturbances was seen in 3 patients with schwannoma (1 permanent) and 2 patients with neurofibroma (both permanent). New sensory deficits were seen in 12 schwannoma patients (7 permanent), 1 neurofibroma patient (0 permanent), and 1 MPNST patient (permanent) (Fig. 1). In both the univariate and multivariate analyses, there were no significant predictors among our collected parameters that were associated with worsened postoperative sensory outcomes.

Pain was reported for 57.9% of schwannomas, 75.5% of neurofibromas, and 68.4% of MPNSTs. This pain was neuropathic in character and in the distribution of the affected nerve in 39.8%, 42.9%, and 42.1% of schwannomas,
neurofibromas, and MPNSTs, respectively. No patient with preoperative neuropathic pain reported worsening pain postoperatively. New postoperative neuropathic pain, in or adjacent to the distribution affected by the resected tumor, was reported by 2 patients with schwannoma (1 permanent), 2 patients with neurofibroma (1 permanent), and 2 patients with MPNST (1 permanent). None of our collected parameters, including tumor histopathology, were associated with worsened postoperative pain scores.

Tumor Recurrence
Among BPNSTs, the overall recurrence rates in our cohort were 5.3% for schwannomas and 8.2% for neurofibromas. Patients with recurrent schwannoma presented to neurosurgical attention on average 49.6 months after their index procedure, while patients with recurrent neurofibromas presented slightly earlier at 41.2 months. In the univariate analyses, a diagnosis of NF3 was associated with increased recurrence risk for schwannomas (OR 4.29, 95% CI 1.05–20.80; p = 0.048), with a recurrence rate of 14.3% in our cohort; a diagnosis of NF1 was associated with increased recurrence for neurofibromas (OR 1.18, 95% CI 1.003–1.39; p = 0.022), with a recurrence rate of 15.4% in our cohort. In the multivariate analyses, STR

<table>
<thead>
<tr>
<th>Location</th>
<th>Schwannoma</th>
<th>Neurofibroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axillary nerve</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ulnar nerve</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Elbow</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Wrist</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Median nerve</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Radial nerve</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Supraclavicular</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Infraclavicular</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic paraspinal plexus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Femoral nerve</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Common sciatic nerve</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Tibial nerve</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Peroneal nerve</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Plantar nerve</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sural nerve</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Lumbosacral plexus</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Occipital nerve</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Vagus nerve</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>22</td>
</tr>
</tbody>
</table>

PIN = posterior interosseous nerve.

TABLE 2. Anatomical locations of 182 BPNSTs

<table>
<thead>
<tr>
<th>Location</th>
<th>Schwannoma</th>
<th>Neurofibroma</th>
</tr>
</thead>
<tbody>
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<td>Axillary nerve</td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
<td>Peroneal nerve</td>
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</tr>
<tr>
<td>Tibial nerve</td>
<td>1</td>
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</tr>
<tr>
<td>Plantar nerve</td>
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<td>Lumbosacral plexus</td>
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<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
<td>22</td>
</tr>
</tbody>
</table>

All values reported as the number of tumors (%).

TABLE 3. Symptomatic presentation of 201 tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Weakness</th>
<th>Numbness/Paresthesia</th>
<th>Tinel's Sign</th>
<th>Pain</th>
<th>Mass Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwannoma</td>
<td>17 (42.8)</td>
<td>40 (40.1)</td>
<td>86 (64.7)</td>
<td>77 (57.9)</td>
<td>30 (22.6)</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>15 (21.3)</td>
<td>22 (22.9)</td>
<td>25 (25.0)</td>
<td>37 (25.5)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>MPNST</td>
<td>7 (35.8 )</td>
<td>5 (26.3</td>
<td>8 (41.2)</td>
<td>13 (68.4)</td>
<td>3 (15.8)</td>
</tr>
</tbody>
</table>

All values reported as the number of tumors (%).
was independently associated with increased recurrence for all BPNSTs (OR 13.16, 95% CI 2.04–83.33; p = 0.007). Age, sex, tumor location, and tumor volume were not significant predictors of recurrence for BPNSTs.

The MPNSTs in our series showed a recurrence rate of 21%, though a lack of neurosurgical follow-up may have diminished the true rate.

**Postoperative Complications**

New postoperative neurological deficits and neuropathic pain are summarized in Fig. 1. Among other complications, wound infections occurred in 4 of 175 patients: 3 superficial infections requiring only oral antibiotics, and 1 deeper infection necessitating surgical washout. In 1 patient, a painful neuroma following resection of a schwannoma of the radial nerve at the elbow required resection at 1 year following the initial procedure. One patient with a plexiform neurofibroma of the brachial plexus experienced significant intraoperative bleeding, for which packing material was left in situ and removed during a second procedure. Dysphagia requiring temporary nasogastric tube feeding was seen in 1 patient following uni-
lateral vagus nerve sacrifice during resection of a brachial plexus neurofibroma. One patient experienced a CSF leak following resection of an infraclavicular brachial plexus neurofibroma, which resolved with lumbar drainage and oversewing of the wound.

**Decision Algorithm**

Based on our, as well as other, large series, a surgical decision algorithm for PNSTs is proposed (Fig. 2). In our series, patients with a confirmed diagnosis of NF1, based on clinical and/or genetic criteria, were typically recommended for surgical excision of even asymptomatic benign-appearing PNSTs, with some variability based on lesion size.

**Discussion**

We present one of the largest single-institution series of symptomatic, surgically treated PNSTs. We aimed to identify predictors of tumor recurrence, extent of resection, and postoperative functional outcomes using multivariate analyses to identify independently associated parameters. To the best of our knowledge, this is only the second large series to explore predictors of outcome using multivariate statistical modeling.

Schwannomas and neurofibromas have a benign histology but may recur locally. The recurrence rates for BPNSTs range from 1.3% to 35.9% in the literature and up to 44% for pediatric plexiform neurofibromas. The recurrence rates for the schwannomas and neurofibromas in our series were 5.3% and 8.2%, respectively. STR has been the most consistently identified predictor of recurrence and was independently and significantly associated with recurrence for both BPMSTs and MPNSTs in our series.

Other clinical, radiographic, and surgical parameters have been variably associated with recurrence or extent of resection. A diagnosis of NF1 has been associated with increased recurrence for neurofibromas in some series and STR of neurofibromas in others. Tumor histopathology has been shown to impact recurrence and extent of resection in some series. Artico et al. showed increased local recurrence in neurofibromas compared with schwannomas, and, in the largest reported series to date, Kim et al. demonstrated decreased GTR rates for neurofibromas, predominantly in their plexiform variants. Vetrano et al., however, found that patients with neurofibromas were at increased risk of postoperative neurological deficits but not recurrence; in their series, increased recurrence of BPNSTs was most associated with longer duration of symptoms prior to resection. Larger tumor size at diagnosis has also been associated with increased recurrence, though primarily in series of malignant PNSTs.

In our series, tumor size was not significantly associated with recurrence. While the schwannomas on average were smaller at presentation than the neurofibromas in our cohort, this difference did not reach statistical significance and may be attributable to differences in tumor location. Proportionally fewer neurofibromas were located in the
extremities, where they may be expected to be symptom-
atically or cosmetically noticeable at a smaller size in com-
parison with neurofibromas in a plexal location, which is
consistent with other reports.\textsuperscript{19} We found that NF type was
significantly associated with recurrence: NF1 for neurofi-
bromas and schwannomatosis (i.e., NF3) for schwannomas.
The increased recurrence risk for NF1-associated neurofi-
bromas persisted when plexiform neurofibromas were ex-
cluded. Patients with hereditary predisposition syndromes
should therefore be monitored more closely for recurrence.
Whether a diagnosis of NF increases the likelihood of an
asymptomatic BPNST that would require future resec-
tion is also uncertain. This question may be answered by
longitudinal follow-up of the entire BPNST cohort. How-
ever, follow-up of asymptomatic patients in our cohort was
largely relegated to primary care physicians, and hence
only surgical outcomes are addressed here.

Interestingly, tumor location influenced the extent of re-
section only for schwannomas in our series, with schwan-
nomas located in an extremity being more readily resected
than plexal tumors likely due to anatomical accessibility.
Schwannomas inherently grow extrinsic to their parent
fascicles while neurofibromas are intertwined with mul-
tiple fascicles of origin and are therefore more difficult to
fully resect irrespective of accessibility, which is a pos-
sible explanation for this finding. Another possibility is
that the impact of tumor location is limited to schwanno-
das due to the disproportionately greater association of
neurofibromas with NF. However, in our cohort 53\% of
neurofibromas were associated with NF1, which is not sig-
nificantly different from other series\textsuperscript{2,15,19,23}; moreover, in
multivariate modeling, tumor location influenced the ex-
tent of resection independently of NF status. Admittedly,
our overall cohort of BPNSTs contains a higher number of
patients with NF than other large series, largely due to
the sizeable subset of schwannomas associated with NF3.
However, our finding that NF3+ is associated with the in-
creased recurrence of schwannomas has been echoed in
other series.\textsuperscript{13} Overall rates of GTR in our cohort were
44.9\% for neurofibromas and 76.7\% for schwannomas,
which are lower than implied by Kim et al. in their large
retrospective series.\textsuperscript{19} All patients in our series received
intraoperative neurophysiological monitoring; Levi et al.
reported an increase in the residual tumor in patients mon-
tored intraoperatively, perhaps accounting for our lower
rates.\textsuperscript{19} Unfortunately preoperative electrodiagnostic
data were not available for all patients in our cohort.

Among the BPNSTs in our series, all patients with a
preoperative motor deficit remained stable or improved
postoperatively. New motor deficits were seen immedi-
ately postoperatively in 10.3\% of schwannomas and 11.8\% of
neurofibromas, which were permanent in 5.2\% and 8.8\%,
respectively. Preoperative sensory disturbances were per-
manently exacerbated in only 1 patient with schwannoma
and 2 patients with neurofibroma. New sensory distur-
bances were seen immediately postoperatively in 12.9\% of
schwannomas and 3.7\% of neurofibromas, which were
permanent in 7.5\% and 0\%, respectively. The rates of post-
operative motor deficit in our cohort are largely in keeping
with the lower end of the range reported in the literature.
In the largest series to date, Kim et al. reported stable or
improved motor function in 89\% of schwannomas and
85\% of solitary neurofibromas;\textsuperscript{15} Levi et al. reported post-
operative motor deficits in 8\% of schwannomas and 5.9\%
of neurofibromas.\textsuperscript{19} In smaller series, permanent post-
operative sensorimotor deficits have been reported in 11\%–
36.7\% of schwanna patients.\textsuperscript{16,22,33}

In our series, GTR and the presence of a preoperative
motor deficit were predictive of stable or improved postop-
eration motor function. The latter is perhaps initially coun-
terintuitive; however, patients with preexisting deficits at-
tributable to a compressive lesion also have the potential
to improve once their lesion is surgically decompressed.
Ujigo et al. identified a preoperative positive Tinel’s sign
as predictive of postoperative sensorimotor deficit, but this
was not observed in our series.\textsuperscript{33} Surgical technique may
also influence postoperative neurological outcomes. Date
et al. espoused the practice of intracapsular enucleation
rather than extracapsular resection of schwannomas lo-
cated in an extremity to minimize postoperative deficits.\textsuperscript{7}
Levi et al. noted that patients with either schwanna or
neurofibroma who had undergone a needle or open biop-
sy procedure prior to definitive resection were at 2.7-fold
higher risk of postoperative neurological deficits than those
who underwent a resective procedure up front.\textsuperscript{19} However,
we were not able to identify in all records whether a biopsy
had been performed at an outside institution.

MPNSTs represent a significant management challenge
for peripheral nerve specialists. They occur mostly in the
trunk and extremities but have been reported rarely at
other sites.\textsuperscript{25,36} Half are associated with NF1, with the re-
mainder arising either de novo (40\%) or secondary to prior
radiation (10\%).\textsuperscript{9,36} While MRI remains the initial workup
of choice for all PNSTs, FDG-PET has shown promise for
accurately differentiating benign from malignant NF1-as-
associated lesions, potentially avoiding the morbidity associ-
ated with surgical biopsy.\textsuperscript{3,10,37}

The primary treatment for MPNST remains wide lo-
cal resection, though limb amputation in the absence of
systemic metastases may be considered. Local recurrence
rates may reach up to 65\%,\textsuperscript{4,39} 5-year tumor-specific sur-
vival ranges from 16\% to 52\%,\textsuperscript{10,31,41} While NF1-associated
MPNSTs have traditionally been associated with a poorer
prognosis than sporadic lesions,\textsuperscript{18,39} a recent meta-analysis
showed no significant differences in overall survival.\textsuperscript{17}
Local recurrence for MPNST in our series was 21\%, well be-
low the rates reported in the literature, though this likely
reflects a loss of neurosurgical follow-up to oncological
specialists. In multiple retrospective series, tumor size (>5 cm), truncal location, incomplete resection, high grade,
S100\()\text{-} negativity, and p53 mutations have been associated
with worse prognosis.\textsuperscript{9,14,31,34,41} In our limited cohort of
MPNSTs without immunohistopathological data available,
STR was the only independent predictor of recurrence.

MPNSTs have traditionally been resistant to adjuvant
chemo- or radiotherapy. Recent studies have demonstrated
improved local control with adjuvant external-beam ra-
diation but a negligible effect on overall survival.\textsuperscript{4,14,34} The
roles of proton-beam therapy and brachytherapy—the lat-
ter is applied widely with good effect on other soft-tissue
sarcomas—have yet to be elucidated for MPNSTs. Con-
ventional chemotherapy for MPNSTs has shown poor re-

Multidisciplinary management of peripheral nerve tumors

Results in trials on vincristine, doxorubicin, ifosfamide, and cyclophosphamide. Genetic and molecular alterations in MPNSTs may classify them into distinct strata, allowing the development of novel targeted therapeutics directed toward oncogenic pathways including mTOR, MEK, and VEGF.4,38

Conclusions

We present here one of the largest surgical series of PNSTs to date. Functional outcomes are influenced by tumor histopathology, while recurrence rates depend on tumor histopathology, genetic predisposition syndrome, and, as demonstrated uniquely by our group, tumor location for certain subtypes. GTR should be attempted for benign lesions where feasible. MPNST remains a significant challenge, with a poor prognosis despite advances in multimodal therapies.

References

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Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

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