Clinical analysis of spinal stereotactic radiosurgery in the treatment of neurogenic tumors

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OBJECT In this study the authors sought to evaluate clinical outcomes after using stereotactic radiosurgery (SRS) to treat benign and malignant spinal neurogenic tumors.

METHODS The authors reviewed a total of 66 procedures of spinal SRS performed between 2001 and 2013 for 110 tumors in 58 patients with spinal neurogenic tumors, which included schwannomas, neurofibromas, and malignant peripheral nerve sheath tumors (MPNSTs). The clinical and radiological findings were evaluated in patients with benign neurogenic tumors. For the 4 patients with MPNSTs, the authors reported overall survival and results of additional immunohistochemical staining to predict the survival difference among the patients.

RESULTS Of the 92 benign neurogenic tumors, 65 tumors that were serially followed up using MRI after SRS showed significant change in mean tumor volume, from a mean of 12.0 ± 2.6 cm3 pre-SRS to 10.8 ± 2.5 cm3 post-SRS (p = 0.027), over an average of 44 months. The local control rate of benign neurogenic tumors was 95.4%. The 34 patients who presented with clinical symptoms of pain showed a significant symptomatic improvement. The initial mean visual analog scale (VAS) score was 6.0 and decreased dramatically to 1.0 after SRS during an average follow-up period of 10.9 months (median of 8.1 months). Although the proportions of transient swelling and loss of intramural enhancement were significantly different among the groups, there was no statistically significant correlation between those 2 factors and local tumor control (p = 0.253 and 0.067, respectively; Fisher’s exact text). Cross-table analysis also indicated that there was no statistically significant relationship between groups with loss of intramural enhancement and transient swelling. The median survival of neurofibromatosis Type 1 (NF1)–related and sporadic MPNSTs was 1.13 and 5.8 years, respectively. Immunohistochemical results showed that S100 was expressed in a sporadic MPNST or neurofibroma, whereas topoisomerase-II alpha was expressed in NF1-related MPNSTs.

CONCLUSIONS SRS is an effective treatment modality for benign neurogenic tumors, while MPNSTs showed heterogeneity in their responses to SRS.

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KEY WORDS stereotactic spinal radiosurgery; spinal neurogenic tumors; malignant peripheral nerve sheath tumor; neurofibromatosis; immunohistochemical staining; oncology

Primary spinal cord tumors account for between 4% and 8% of CNS neoplasms. Schwannomas and neurofibromas, also known as peripheral nerve sheath tumors or neurogenic tumors, account for 25% of intradural extramedullary neoplasms. Malignant peripheral nerve sheath tumors (MPNSTs) constitute about 5% of malignant soft-tissue tumors, and 67% of these tumors arise from neurofibromas. Most benign neurogenic tumors are noninfiltrative; therefore, microsurgical resection remains the treatment of choice. However, for patients who are not suitable candidates for surgery, including older patients, patients with comorbidities, those with recurrent or multiple tumors, and those with familial phakomatoses such as neurofibromatosis (NF), stereotactic radiosurgery (SRS) is an important treatment option. With the recent advent of radiosurgical treatment, spinal
SRS is now widely used for the treatment of CNS neurogenic tumors. In this study we analyzed the clinical and radiographic outcomes of spinal SRS in the treatment of both benign and malignant spinal neurogenic tumors. We also conducted an immunohistochemical investigation to estimate the prognostic relevance of neurofibromatosis Type 1 (NF1)–related and sporadic MPNSTs.

**Methods**

This study included all 58 patients diagnosed with spinal neurogenic tumors who underwent SRS using the Novalis Radiosurgery platform (Brainlab GmbH) between 2001 and 2013 at our institution. A total of 66 spinal SRS procedures were performed for 110 tumor lesions in 58 patients. Of these lesions, 92 were benign and 18 were malignant spinal neurogenic tumors. Forty-seven patients harbored schwannomas, 7 had neurofibromas, and 4 harbored MPNSTs. Patients’ demographic information is included in Table 1. Clinical symptoms were obtained and evaluated, using patients’ charts. Pain was measured using a visual analog scale (VAS).

Magnetic resonance imaging follow-up was performed in 41 of the 54 patients (a total of 65 tumors) with benign neurogenic tumors. Thirteen patients with benign tumors who were lost to imaging follow-up or for whom the duration of follow-up was less than 12 months after SRS were excluded from this radiological analysis. The mean follow-up period was 43.2 months (range 12–136.8 months). Tumors were evaluated radiologically, and the gross tumor volume (GTV) before and after SRS was measured using iPLAN treatment planning software (Brainlab).

The indications of SRS were determined in consideration of various factors including residual and/or recurrent tumors, a separation surgery to decompress the spinal cord, the tumor location, patient age and medical conditions, and patient preference. SRS was used as the primary treatment modality in 39 patients. The remaining patients with benign tumors were treated using a combination of surgery and SRS. The image-guided spinal SRS procedure was performed after the patient was placed on a body vacuum cushion in an ExacTrac body tray with an aquaplastic mask frame under a real-time infrared tracking system (ExacTrac, Brainlab). High-resolution MRI was performed in all patients. After the image fusion procedure using MRI and stereotactic-equipped CT imaging was performed, radiosurgical planning was performed using BrainScan (version 5.31, BrainLAB) or iPLAN software (version 4.1.1). The prescription dose, which varies by tumor volume and location, was delivered into the tumor margin using the 80% isodose line. The median tumor volume was 6.0 cm³ for schwannomas, 0.2 cm³ for neurofibromas, and 19.3 cm³ for MPNSTs. The median prescribed dose was 13 Gy in a single session for benign neurogenic tumors (average volume of 8.5 cm³); however, hypofractionated SRS (median 25 Gy in 5 fractions) was performed for the large benign tumors (average GTV 77 cm³, median 53 cm³). For malignant tumors, a higher dose of 40 Gy was applied to margins in 5 fractions. For the majority of cases, we used a single isocenter to treat an individual tumor. In some selected cases, however, we used 2 or 3 isocenters, depending on the clinical conditions including tumor location, shape, size, and distance between adjacent tumors.

**Outcome Analysis**

The overall clinical outcomes of patients with benign neurogenic tumors were analyzed, and the local tumor control rate was measured according to the radiographic analysis. Furthermore, contingency table analysis using the chi-square test and Fisher’s exact test were performed among a total of 65 benign lesions to evaluate local tumor control–related factors, which included age, volume, histopathology, sex, loss of intramural gadolinium enhancement, and transient swelling. A p value < 0.05 indicated

| TABLE 1. Demographic features of patients included in the study |
|------------------|-----------------|-----------------|-----------------|
| Variable         | Benign          | Malignant       |
|                  | Schwannoma*     | NF1             | Total           | MPNST           |
| No. of patients  | 47              | 7               | 54              | 4               |
| No. of lesions   | 69              | 23              | 92              | 18              |
| Single           | 38              | 3               | 41              | 0               |
| Multiple (no. of patients) | 31 (9) | 20 (4) | 51 | 18 (4) |
| GTV in cm³       |                 |                 |                 |                 |
| Median           | 6.0             | 0.2             | 19.3            | 4.98–139.4      |
| Range            | 0.03–340.04     | 0.07–3.33       |                 |                 |
| Symptoms & signs |                 |                 |                 |                 |
| Pain             | 30              | 4               | 34 (63%)        | 1               |
| Neurological     | 11              | 2               | 13 (24%)        | 3               |
| Incidental       | 6               | 1               | 7 (13%)         | 0               |
| Treatment        |                 |                 |                 |                 |
| SRS alone        | 35              | 4               | 39 (72%)        | 0               |
| Surgery+SRS      | 12              | 3               | 15 (28%)        | 0               |
| Multimodal†      | 0               | 0               | 0               | 4               |

* Includes 3 patients with NF2.
† Combined surgery with or without radiotherapy and/or chemotherapy.
statistical significance. All analyses were performed using SPSS statistical software (version 21.0, IBM).

For the 4 patients with MPNSTs, a cumulative survival rate was estimated using the Kaplan-Meier method. In addition, immunohistochemical analysis was performed to examine the differences in outcome between NF1-related and sporadic MPNSTs.

Immunohistochemical Staining

Immunohistochemical staining for topoisomerase II alpha (TOP2A) and S100 from the 4 MPNSTs and 1 cutaneous neurofibroma from a patient with multiple cutaneous NF1 (which was used as a control sample) was performed. The antibodies for immunohistochemistry were as follows: an anti–TOP2A antibody (dilution 1:100, mouse monoclonal; NeoMarkers) and an anti–S100 antibody (1:400, rabbit polyclonal; Zymed).

The percentage of positive cells was evaluated in the highest expression area. For TOP2A, nuclear positivity of more than 50% of the cells was considered +3, 30%–50% +2, and 10%–30% +1 positive. For S100, both nuclear and cytoplasmic positivity of the cells was considered positive. The quantitation method is the same as that for TOP2A.

Results

Clinical Outcomes of Benign Neurogenic Tumors

After treatment, most of the patients achieved stability or showed improvement in clinical symptoms. There were no notable radiation-related complications after SRS during the follow-up period. There was significant improvement in VAS score after SRS among the 11 patients whose symptom was moderate-to-severe pain prior to treatment. During a median period of 8.1 months, the mean VAS score improved from 6.0 before SRS to 1.0 after SRS. The remaining 23 patients with less pain also achieved stability or some improvement after treatment. All neurologically compromised patients who underwent surgery experienced improvement after surgery and subsequent SRS.

Radiological Analysis of Benign Neurogenic Tumors

In radiological analysis, 41 patients (65 lesions; 32 in patients with 1 lesion and 33 in the 9 patients with multiple lesions) were analyzed. The mean follow-up period was 43.2 months, (range 12–136.8 months). The total mean volume of these 65 tumors in all 41 patients was 12.0 ± 2.6 cm³ pre-SRS and 10.8 ± 2.5 cm³ post-SRS (p = 0.027); (Fig. 1A).

The change in volume was defined as follows: decreased volume as a greater than 10% decrease in volume, stable or no change as a less than 10% volume change, and increased tumor volume as a greater than 10% increase in volume. Thirty-six (55.4%) of the 65 lesions were classified as decreased in volume (Fig. 1B), 26 (40.0%) as no change (Fig. 1C), and 3 as increased in volume (Fig. 1D). Thus, local tumor control was attained in 62 of the 65 lesions (95.4%) (i.e., the decreased volume and no change groups). MRI scans obtained in patients with a single lesion were additionally analyzed for intratumoral necrosis, defined as a loss of intratumoral signal intensity of the gadolinium enhancement and high signal on T2-weighted imaging. A total of 22 single-lesion patients presented with loss of intramural enhancement. In the local tumor control group, 11 of 17 patients (64.7%) in the decreased tumor volume change group and 8 of 12 (66.7%) in the no change group showed intratumoral necrosis; in the increased volume group, all patients showed loss of intramural enhancement, which implied intratumoral necrosis. A contingency table analysis of multiple factors affecting local tumor control is summarized in Table 2. Although the proportions of transient swelling and loss of intramural enhancement were significantly different among the groups, there was no statistically significant correlation between those 2 factors and local tumor control (p = 0.253 and 0.067, respectively, Fisher’s exact test; Table 2). Cross-table analysis also indicated that there was no statistically significant relationship between groups with loss of intramural enhancement and transient swelling (Table 3).

Cases of Local Failure

An increase in tumor volume was defined as local treatment failure and was seen in 3 of the 41 patients who underwent radiological analysis (Fig. 1D). One of the patients showed a good tumor control response for 4 years, but eventually developed late-onset intratumoral necrotic cyst enlargement during an 8-year follow-up. The other 2 patients showed radiographic signal change, which was loss of intramural enhancement as early as 6- and 18-month follow-up MRI after SRS. While one patient was later lost to follow-up (Fig. 2), the others continued with follow-up, and showed asymptomatic conditions and no complications related to collateral damage of irradiation, showing only an enlargement of intramural necrosis that subsequently remained stable.

Clinical Outcomes and Kaplan-Meier Survival Analysis of MPNSTs

In the treatment of patients with MPNSTs either NF1-related or sporadic type, the results were widely variable. In the present series, patients with NF1-related MPNSTs had worse outcomes than those with the sporadic type. In addition, 3 patients with MPNSTs were previously diagnosed as having NF1. Two patients had coincidental MPNSTs at other body sites; however, following radiosurgical treatment of other NF lesions, the tumor showed rapid progression. Both patients had advanced NF with multiple spinal neurofibromas and tumors (Fig. 3). Despite systemic chemotherapy for these 2 patients, the rapid disease progression led to death. These findings of unexpected rapid disease progression to death or the worst outcome were attributed to malignant transformation of neurofibroma into MPNST resulting in rapid tumor progression and systemic metastases triggered by irradiation. In the remaining patient, SRS was performed to the postoperative residual MPNST tumor; however, the patient was lost to follow-up. The median survival time of patients with NF1-related MPNST was 1.13 years, while survival the length for those with the sporadic type was 5.8 years (Fig. 4). The patient with sporadic MPNSTs showed regional progression more frequently than local recurrence or treatment failure, and this was treated with repeated SRS. Despite the high incidence of regional recurrences.
of the tumors, repeated SRS achieved local tumor control, which increased the patient’s survival by 3 years for an overall cumulative survival of 5 years after diagnosis.

Results of Immunochemical Staining of the Four MPNSTs

Immunohistochemical stains showed that TOP2A was expressed in 2 cases of NF1-related MPNST and negativity of both TOP2A and positive S100 expression in remaining case of NF1-related MPNST. However, a case of sporadic MPNST showed both negativity of TOP2A and positive expression of S100 (Table 4 and Fig. 5). Although the number of cases was small, either positivity of TOP2A or negativity of S100 may be associated with poor prognosis.

Discussion

The clinical experiences with spinal SRS have been used in the treatment of benign spinal intradural extramedullary tumors, such as meningiomas, schwannomas, and neurofibromas, since 1999. The first report of hypofractionated SRS for spinal lesions was published in 2001. Since 2006, an increasing number of uses of spinal SRS in the treatment of benign neurogenic tumors has been reported. Dodd et al. reported 39 neurogenic tumors (30 schwannomas and 9 neurofibromas) in 2006 for a median follow-up period of 36 months. Sachdev et al. reported 71 cases of neurogenic tumors (47 schwannomas and 24 neurofibromas) in 2011 for a median follow-up period of 33 months. Local control of schwannoma and neurofibroma was 98% and 100%, respectively. In the present study, benign neurogenic tumors showed a 95.4% local control rate.

The local control rate in the literature ranges between 95% and 100% under the minimal toxicity using single-to-hypofractionated SRS with a median follow-up of longer than 2 years. Clinical results of spinal SRS have been favorably compared with the results from cranial SRS for benign CNS tumors in terms of the effectiveness and safety for the treatment of benign spinal tumors. The long-term local control rate of vestibular schwannomas has been well documented as 95%–98% at 10 years.

Typical Radiographic Response and Local Failures After SRS

The radiographic response of the benign neurogenic tumors invariably shows several distinct patterns: tumor regression with or without transient swelling, stable, initial tumor enlargement followed by stability, and progressive enlargement. Similar findings have been observed in previous studies of vestibular schwannomas following
SRS.6,7,16 One study concerned a transient volume increase or swelling as pseudoprogression (23%, 17 patients), which defined a responder of initial progression followed by stabilization of the change.6 In that series, 12% (9 patients) of vestibular schwannomas showed progressive tumor growth, which implied treatment failure, and 3 patients required subsequent resection. One patient showed only early tumor progression; however, the remaining patients presented with enlargement 24 months later.6 The volumetric response in vestibular schwannomas showed that tumor enlargement following SRS appears at 4–6 months with a median of 9 months, ranging from 4 to 60 months.6,11,16 The incidence of progressive tumor enlargement was 14% (30 of 208 patients over 15 years).16 Among a total of 30 patients with tumor enlargement, 93% (28 patients) showed a loss of central enhancement and 20% (8 patients) had new neurological symptoms. However, about 57% (16) of the patients showed subsequent regression by 24 months. Only 14% (4) of the patients required additional treatments, including surgery and SRS.16

In our previous radiographic study,6 transient swelling was observed in 37% of tumors. Although the volumetric analysis for 35 neurogenic tumors in 28 patients included

### Table 2. Multiple factor analysis for contingency tables related with local tumor control in the treatment of SRS for spinal benign neurogenic tumors (n = 65)*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Local control (%)</th>
<th>p Value</th>
<th>% in Groups A/B/C†</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60 vs &gt;60</td>
<td>86.2 vs 14.5</td>
<td>1.000‡</td>
<td>57.1/37.5/5.4</td>
<td>0.747</td>
</tr>
<tr>
<td>Vol in cm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3.1 vs &gt;3.1</td>
<td>49.2 vs 50.8</td>
<td>0.114</td>
<td>53.1/37.5/9.4</td>
<td>0.195</td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schwannoma vs NF</td>
<td>86.2 vs 13.8</td>
<td>0.072</td>
<td>57.1/37.5/4.4</td>
<td>0.747</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male vs Female</td>
<td>56.9 vs 43.5</td>
<td>0.727</td>
<td>54.1/40.5/5.4</td>
<td>0.845</td>
</tr>
<tr>
<td>Loss of intramural enhancement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent vs Present</td>
<td>58.5 vs 41.5</td>
<td>0.067</td>
<td>69.5/39.5/0</td>
<td>0.108</td>
</tr>
<tr>
<td>Transient swelling Absent vs Present</td>
<td>43.1 vs 56.9</td>
<td>0.253</td>
<td>89.3/10.7/0</td>
<td>0.000</td>
</tr>
</tbody>
</table>

* Values in boldface are statistically significant.
† Groups A, B, and C were defined as the tumors with decreased, stable, and increased tumor volume, respectively, after radiosurgery. Group A corresponds to Fig. 1B, Group B corresponds to Fig. 1C, and Group C corresponds to Fig. 1D.
‡ Fisher’s exact test.
§ Pearson’s chi-square test.

### Table 3. Cross-table analysis showing the factors of transient swelling and loss of intramural gadolinium enhancement after SRS in 65 tumors

<table>
<thead>
<tr>
<th>Transient Swelling</th>
<th>Loss of Intramural Enhancement</th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>19 (67.9%)</td>
<td>32 (12.1%)</td>
<td>43.1%</td>
</tr>
<tr>
<td>Present</td>
<td>19 (51.4%)</td>
<td>18 (48.6%)</td>
<td>56.9%</td>
</tr>
<tr>
<td>Total</td>
<td>58.5%</td>
<td>41.5%</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Fisher’s exact test.
† Pearson’s chi-square test.
2 MPNSTs, it was found that the intratumoral necrosis was related to a transient swelling, which tends to correlate with long-term tumor shrinkage after SRS. Therein, we measured volumetric analysis for 65 benign neurogenic tumors in 41 patients and found that the intratumoral necrosis was seen not only in the group with local tumor control but also in the group with tumor enlargement, as shown in the clinical series of SRS for vestibular schwannomas.

In the treatment of benign neurogenic tumors, tumor enlargement after SRS is considered to induce intramural changes with necrosis and cystic development resulting from intratumoral bleeding rather than local relapse of tumor. Symptomatic enlargement often requires surgical intervention; however, a stable lesion in spite of an initial increase in volume may continue to follow-up unless it becomes asymptomatic or progressing. In the present series, one patient exhibited tumor enlargement by 11%–36% at 18- to 31-month MRI follow-up, followed by volume stability at 43 months. Another patient (Fig. 2) showed tumor enlargement by 32% at 22 months who was then lost to follow-up. The third patient showed local tumor control with intramural necrosis at 4 years of follow-up MRI and then developed asymptomatic cystic enlargement of intramural necrosis on the 8-year follow-up imaging study. One patient was lost to follow-up, while the remaining 2 are undergoing continuing observation. All 3 lesions showing increased tumor volume showed significant intramural necrosis, which implied transient swelling with or without myxoid degeneration, and delayed intratumoral hemorrhage resulting in cystic development and enlargement.

The Clinical Response of SRS for the Neurogenic Tumors in Neurofibromatosis

Schwannomas are the most common spinal tumors that occur in patients with neurofibromatosis Type 2 (NF2), an autosomal-dominant genetic disorder that predisposes patients to developing multiple central and peripheral nervous system tumors. The tumors associated with NF2 are more aggressive and recur more often after treatment.

In a retrospective review of 87 patients with spinal nerve sheath tumors that were surgically removed, 17 of whom had NF2-associated schwannomas, all NF2-related tumors recurred in 9 years compared with a 10-year recurrence rate of 28% in tumors not associated with NF2. This study found that the factors that correlated with recurrence
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after surgery were partial resection, prior recurrence, NF2, and advanced age.

Unlike schwannomas, neurofibromas arise more commonly in the ventral nerve root. Neurofibromas are benign peripheral nerve sheath tumors consisting of Schwann cells often found in patients with NF1. The most common neurofibromas associated with NF1 are a localized cutaneous type that are usually indolent and painless followed by localized intraneural neurofibromas of plexiform type, which can be located anywhere from the spinal and cranial nerve roots to the peripheral nerves. Although microscopic surgical excision is the treatment of choice for benign neurogenic tumors, recently SRS is becoming an important treatment option in the selected patients who expect high surgical or medical morbidity or repeated and/or invasive surgery.

Clinical response of SRS varies according to the pathologies in neurofibromatosis. Sahgal et al. documented local progression of 2 neurofibromas in the patients with NF1. They suggested the dose-response relationship might be related to tumor control and its clinical outcome in neurofibroma. Dodd et al. reported the results of SRS for spinal schwannomas including 40% of NF2-related type schwannomas; 41% of these patients were treated for recurrent or residual tumors after surgery. In their series, among the 9 tumors in 7 NF1 patients, 50% showed symptom progression, such as pain, weakness, and numbness, after SRS. One patient had to undergo surgery 13 months after SRS. The authors assumed that the poor results of SRS in patients with NF1 were related to multiplicity of offending nerve roots and relatively larger size of the tumors compared with other patients with neurogenic tumors.

In the present study, there were 3 NF2 patients with multiple schwannomas and 7 patients with NF1. The tumor lesions became stable or regressed, and the presenting symptoms were stable or improved after SRS.

MPNSTs

MPNSTs arise from a peripheral nerve or demonstrate nerve sheath differentiation. They may occur in association with NF1, may be the consequence of previous radiation therapy (radiotherapy-induced), or may occur sporadically. While earlier studies estimated that the lifetime risk of developing MPNST for an NF1 patient is 1%–2%, more recent analyses found the risk to be 8%–13%. This discrepancy in the data may be attributed to the underdiagnosis of NF1, as a reported 20%–50% of patients with MPNST have NF1.

Currently, the accepted treatment for MPNST is surgery, but resectability depends largely on the location of the tumor and ranges from 20% in paraspinal MPNST to 95% in tumors of the extremity. A negative surgical margin is the most significant factor for survival and local control of MPNSTs, and a complete surgical removal remains the most effective treatment. However, in cases of spinal MPNST, due to proximity of surrounding critical structures, en bloc resection is usually difficult. Therefore,

FIG. 5. Comparison between sporadic and NF1-related MPNSTs of TOP2A and S100 stain. TOP2A expression is negative (A) but S100 protein is strongly positive (B) in sporadic MPNST; in contrast, either TOP2A is positive (C) or S100 protein expression is negative (D) in NF1-related MPNSTs. Figure is available in color online only.
adjuvant or additional therapy for MPNST is often needed. Many authors have suggested that auxiliary radiotherapy may enhance the local control of MPNSTs. A study by Wong et al. suggested that radiotherapy using a dose greater than 60 Gy is effective for local control of MPNST. In addition to the previously stated factors that affect prognosis of MPNSTs in terms of tumor size, location, histological grade, and feasibility of en bloc or complete resection, other factors reported to influence prognosis include association with NF1, nuclear expression of p53, and expression of S100.

The 5-year survival of patients with MPNSTs varies between studies, ranging from 34% to 52%. Past reports show that NF-related MPNSTs are associated with a markedly shorter survival time than sporadic MPNSTs. Our experience agrees that patients with sporadic MPNSTs have significantly better survival outcomes than those with NF-related MPNSTs. However, a recent meta-analysis by Kolber et al. suggested that there is no statistically significant difference between survival of MPNST patients with and without NF, and noted a correlation in published studies between larger patient samples and a smaller difference in outcomes of MPNST patients with and without NF. Therefore, we conclude that more multivariate and compiled analyses are necessary to further evaluate the relationship between survival times and NF-association in MPNSTs.

Despite our small sample size, we performed additional immunohistochemical staining to estimate a patient’s prognosis according to previously reported literature. As shown in Table 4, S100 positivity is associated with sporadic MPNSTs and showed a better survival length, while TOP2A is expressed in NF1-related MPNSTs and is associated with a shorter survival length after radiosurgical procedure. This result was compatible to previous studies. Furthermore, the prognostic factors of MPNSTs will be compiled and need to be evaluated.

Conclusions
Spinal SRS is a safe and effective, noninvasive treatment modality in the treatment of benign neurogenic tumors. Although SRS offers a good local tumor control rate (95.4%), 20% of benign neurogenic tumors (13 of 65 lesions) showed an increase in volume during the first median time period of 8 months (range 5.1–44.3 months) following treatment, and then eventually regressed in volume. Our data also showed poorer outcomes with NF1-related MPNST than with sporadic-type MPNST. Immunohistochemical analyses performed in samples obtained from our patients suggest a correlation between malignant tumor development and downregulation of S100 and upregulation of TOP2A. Treatment of MPNSTs using SRS is still challenging, and more investigations are needed.

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