Stereotactic Radiosurgery for Spine Tumors: Review of Current Literature

Wesley Hsu  Trang Nguyen  Lawrence Kleinberg  Eric C. Ford  Daniele Rigamonti  Ziya L. Gokaslan  Michael Lim

Department of Neurosurgery, Johns Hopkins Medical Institutions, Baltimore, Md., USA

Key Words
Spine tumor · Spinal cord tumor · Radiosurgery · Metastatic spine disease · Stereotaxy

Abstract
Stereotactic radiosurgery (SR) is increasingly utilized for the treatment of intracranial and extracranial pathology. It is considered an important adjuvant to surgery, chemotherapy or fractionated radiotherapy, and the role of SR as a primary treatment modality continues to be explored. SR was recently defined as using ‘externally generated ionizing radiation … to inactivate or eradicate (a) defined target(s) in the head or spine … performed in a limited number of sessions, up to a maximum of five’ [1]. SR was first conceived by Lars Leksell [2] as a potential tissue ablation modality for intracranial functional neurosurgery. Collateral damage to adjacent structures was occasionally problematic with the early use of SR, but improved stereotactic imaging allowed for better target localization and delineation of adjacent structures [3]. The use of computer-aided tracking systems improved targeting of radiation while excluding normal tissue [4]. Collectively, these advances improved the accuracy and efficacy of SR for intracranial lesions while limiting treatment morbidity. SR is now well established as having a role in the treatment of intracranial disease [5, 6].

During the mid-1990s, investigators sought to expand the scope of SR to extracranial pathology, specifically tumors of the spine. In 1996, Hamilton et al. [7] first reported the use of SR for spinal pathology using a linear accelerator. Further improvements in frameless stereotactic technology also allowed for advanced targeting ca-
Stereotactic techniques offer improved treatment capabilities for spinal lesions [8, 9]. Initially, targeting was based on fiducial localization systems (often using implanted screws) for tumors in or around the mobile spine. Today, computer-aided guidance systems can recognize skeletal structures in the vicinity of the target area, thereby obviating the need for fiducials while allowing for adjustments during the treatment session to account for movement of the spine during SR.

The most commonly used SR machines include Synergy S (Elekta), Novalis (Brainlab) and Cyberknife. All use computed-tomography-based technology for treatment planning. Novalis and Cyberknife also use serial radiographs performed during SR treatment to identify any movement of the spine and change SR targeting accordingly. Synergy S and Novalis utilize a mobile table to change targeting coordinates, while Cyberknife utilizes a mobile robotic arm. Data suggest that all systems have excellent accuracy, and studies suggest that targeting areas are probably close to 1 mm [9–12]. For example, Cyberknife was found to have a clinically relevant accuracy of 0.7 ± 0.3 mm [12]. Such systems minimize radiation exposure to the spinal cord and allow for the safe application of high doses of radiation to the target area [12].

Although SR for spinal lesions is in its infancy, there is a growing body of literature supporting its efficacy. The purpose of this review is to summarize the pertinent literature regarding the use of SR for lesions of the spine and spinal cord. Particular emphasis will be placed on large clinical series of both primary and secondary spine tumors.

**SR for Metastatic Spine Disease**

Metastatic spinal disease continues to be the cause of significant morbidity, as 40% of all cancer patients develop spinal metastases [13]. SR is currently well established as having a role in the treatment of intracranial metastatic disease [5, 6]. The experience gained using SR for intracranial metastatic disease is now being translated to metastatic spine tumors (fig. 1). There are currently several large institutional series documenting the efficacy of SR for spinal metastatic disease [14–24] (table 1).

Gerszten et al. [14] reported the largest series of spine tumors treated with SR. A total of 393 patients were treated for 500 lesions involving the vertebral body. The vast majority were metastatic lesions. Of the 336 patients with pain as the primary indication for SR, 86% experienced long-term improvement in pain control. Pain control was more likely with certain tumor histology (breast, melanoma, renal and lung cancer). 88% of patients had radiographic evidence of local control. Interestingly, no patients had evidence of tumor progression at adjacent vertebral body levels. Nelson et al. [24] did not find adjacent level treatment failures in their series of 32 patients either. In contrast, Ryu et al. [25] reported that 4% of patients developed progression at adjacent vertebral levels in their series. When tumors do recur, it appears that they come back near the spinal cord. Chang et al. [21] found that the most common location of recurrence was the epidural space (47%) followed by the pedicles and posterior elements (18%). This suggests that the recurrence was along the portion of the tumor receiving the

![Fig. 1. Computed tomography images (axial, sagittal, coronal) with superimposed spinal stereotactic dosage plan of a metastatic adrenal adenocarcinoma lesion in the L3 vertebra.](image-url)
smallest dose or, perhaps, could have been a marginal miss [21].

Overall, the studies suggest that SR appears to provide excellent local control for metastatic spine cancer. All but 1 study report a greater than 80% local control rate. De Salles et al. [17] report the lowest rate of local control (56%). However, in closely examining their series, 93% of patients were previously radiated, and 50% had prior surgical intervention for these lesions. In contrast, studies such as that by Degen et al. [22] reported 100% local control in patients who had no prior radiation treatment. Also, Amdur et al. [20] reported in their prospective series of 21 patients with metastatic spine cancer that 95% of treated lesions were locally controlled after SR therapy. The high rate of local control may be partially explained by the short survival time of this cohort, as the median survival was only 8 months [20].

In terms of pain control, SR appears to have excellent efficacy in improving pain attributable to metastatic disease. A large proportion (43–97%) of patients experienced improvement in back pain after SR. This data is comparable to that reported for patients receiving standard fractionated radiotherapy for spine metastases [26].

SR appears to also reverse neurological decline. Gerszten et al. [14] reported that patients experienced improvement in radiculopathies. However, the efficacy of SR in reversing preexisting neurological decline from cord compression is unclear. Many studies have excluded patients with metastatic spine tumors that lead to significant spinal cord compression. Milker-Zabel et al. [23] report that 42% of patients obtained improvement in neurological symptoms after SR. In contrast, Nelson et al. [24] report that none of the 7 patients with neurological deficits from cord compression improved after SR.

## Side Effects

Overall morbidity that is directly attributable to SR is quite low. Decline in neurological function after SR is usually a manifestation of tumor progression rather than radiation toxicity. In the review by Benzil et al. [16] of 31 patients with SR, 2 patients developed radiculitis after SR. Both patients had biologically effective dose values greater than 60 Gy. Ryu et al. [19, 25] recently updated their institutional series of patients with metastatic spine cancer treated with SR. 177 patients were treated for 230 lesions using single-dose SR (8–18 Gy). Of the 86 patients who were alive after 1 year, only 1 patient experienced radiation-induced myelopathy [19, 25].

Vertebral compression fracture is another phenomenon that has occurred after SR [18, 21, 25]. Although they are thought to occur secondary to tumor progression, compression fractures have been documented after SR in patients without evidence of tumor progression [18]. While some believe that the treated vertebral body is structurally weaker, thereby predisposing the individual to a lower threshold of axial stress to cause a compression fracture, the mechanism of fracture has yet to be fully defined.

## SR for Benign Intradural Spine Tumors

With the success of SR for metastatic spine tumors, clinicians have sought to expand the role of SR to primary spine tumors. Of particular interest are intradural tumors such as schwannomas, neurofibromas and meningiomas. The primary treatment option for the vast majority of intradural spine tumors continues to be surgical resection. The efficacy of surgical resection is well reported in the literature [27–31]. However, patients with significant comorbidities may not be able to tolerate surgical resection. Patients with multiple lesions throughout the craniospinal axis, as in the case of some patients with phakomatoses such as neurofibromatosis, may require extensive surgical resection with a significant risk of morbidity. In such patients, SR may be a useful treatment option. Patients who undergo incomplete surgical tumor resection may also potentially benefit from postoperative SR [32].

There are few large series in the literature regarding the outcome of intradural spinal tumors after SR (table 2). Gerszten et al. [34] report the largest series that includes 73 patients with benign spinal tumors (meningioma, schwannoma, neurofibroma). Local control was seen in 99% of tumors, and 70% of patients had improvement in pain control. Three patients developed SR-related neurological complications 5–13 months after treatment. All 3 lesions were located in the cervical spine [34].

Selch et al. [37] reported their series of 20 patients with benign nerve sheath tumors treated with SR. All patients had local control over a median follow-up of 18 months. Two patients experienced radiculopathy that resolved with conservative treatment [37].

Dodd et al. [33] reviewed 51 patients with 55 benign spinal tumors treated with radiosurgery. Local control was established in 98% of lesions. The authors note that only 39% of lesions decreased in size after SR and warn that SR may not be effective in reversing the mass effect produced by these tumors. Twelve patients in their series...
presented with some degree of myelopathy secondary to cord compression from the tumor. Two of these patients required surgical intervention after SR because of persistent myelopathy[33]. The authors also note that patients with neurofibromas failed to achieve significant improvement in preoperative clinical symptoms after SR. This is in contrast to clinical outcomes of patients with meningiomas or schwannomas in their series. This observation mirrors the outcomes of spinal neurofibroma after surgical resection[31].

Sahgal et al.[36] reviewed their series of benign spinal tumors, 14 of which were primary intradural lesions. Of patients with tumors causing pain, 46% experienced improvement in pain after SR. Included in their series were

Table 1. Stereotactic radiosurgery for metastatic spine disease

<table>
<thead>
<tr>
<th>Authors and year</th>
<th>Number of patients/lesions</th>
<th>Age, years</th>
<th>Intra/extra/ metastatic lesions</th>
<th>Method</th>
<th>Mean follow-up months</th>
<th>Tumor volume, cm³</th>
<th>Prior treatment, % surgery radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amdur et al.[20], 2009</td>
<td>21/25</td>
<td>&gt;18</td>
<td>0/3/22</td>
<td>Elekta synergy</td>
<td>2–27 (median 8)</td>
<td>n.r.</td>
<td>0</td>
</tr>
<tr>
<td>Benzil et al.[16], 2004</td>
<td>31/35</td>
<td>40–82 (mean 61)</td>
<td>4/5/26</td>
<td>Novalis</td>
<td>n.r.</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>Chang et al.[21], 2007</td>
<td>63/74</td>
<td>21–82 (median 59)</td>
<td>0/0/74</td>
<td>Exact Varian</td>
<td>0.9–49.6 (median 21.3)</td>
<td>1.6–358 (mean 37.4)</td>
<td>38</td>
</tr>
<tr>
<td>De Salles et al.[17], 2004</td>
<td>14/22</td>
<td>48–82 (mean 60.2)</td>
<td>3/0/19</td>
<td>Novalis</td>
<td>1–16 (median 6.1)</td>
<td>0.75–91.8 (mean 25)</td>
<td>50</td>
</tr>
<tr>
<td>Degen et al.[22], 2005</td>
<td>51/72</td>
<td>mean 53</td>
<td>0/14/58</td>
<td>Cyberknife</td>
<td>mean 12</td>
<td>mean 115</td>
<td>0</td>
</tr>
<tr>
<td>Gerszten et al.[14], 2007</td>
<td>393/500</td>
<td>18–85 (mean 56)</td>
<td>0/0/500</td>
<td>Cyberknife</td>
<td>3–53 (median 21)</td>
<td>0.2–264 (mean 46)</td>
<td>2</td>
</tr>
<tr>
<td>Jin et al.[15], 2007</td>
<td>196/270</td>
<td>n.r.</td>
<td>0/0/270</td>
<td>Novalis</td>
<td>n.r.</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>Milker-Zabel et al.[23], 2003</td>
<td>18/19</td>
<td>16–76 (median 55.2)</td>
<td>0/0/19</td>
<td>n.r.</td>
<td>3.5–33.1 (median 12.3)</td>
<td>20.8–734.9 (median 111.2)</td>
<td>0</td>
</tr>
<tr>
<td>Nelson et al.[24], 2009</td>
<td>32/33</td>
<td>45–82 (median 60)</td>
<td>0/1/32</td>
<td>Novalis</td>
<td>n.r.</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>Ryu et al.[19], 2007</td>
<td>177/230</td>
<td>14–85 (median 61)</td>
<td>0/0/230</td>
<td>Novalis</td>
<td>0.5–49 (median 6.4)</td>
<td>3.4–217 (mean 57)</td>
<td>0</td>
</tr>
<tr>
<td>Yamada et al.[18], 2008</td>
<td>93/103</td>
<td>38–91 (median 62)</td>
<td>0/0/103</td>
<td>n.r.</td>
<td>2–45</td>
<td>n.r.</td>
<td>0</td>
</tr>
</tbody>
</table>

Target doses given in grays. Intra = Intradural primary tumor; extra = extradural primary tumor; n.r. = not recorded; PTV = planning target volume; LC = local control; OS = overall survival; PI = pain improvement; RT = radiation therapy; NNU = narcotic usage fell from 60 to 36% in 6 months.

Table 2. Stereotactic radiosurgery for benign intradural tumors

<table>
<thead>
<tr>
<th>Authors and year</th>
<th>Number of patients/lesions</th>
<th>Age, years</th>
<th>Intra/extra/ metastatic lesions</th>
<th>Method</th>
<th>Mean follow-up months</th>
<th>Tumor volume, cm³</th>
<th>Prior treatment, % surgery radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dodd et al.[33], 2005</td>
<td>51/55</td>
<td>12–86 (mean 46.5)</td>
<td>55/0/0</td>
<td>Cyberknife</td>
<td>6–73 (median 25)</td>
<td>0.14–24.6</td>
<td>51</td>
</tr>
<tr>
<td>Gerszten et al.[34], 2008</td>
<td>73/73</td>
<td>18–85 (mean 44)</td>
<td>73/0/0</td>
<td>Cyberknife</td>
<td>8–71 (median 37)</td>
<td>0.3–93.4</td>
<td>26</td>
</tr>
<tr>
<td>Ryu et al.[35], 2003</td>
<td>7/10</td>
<td>19–61 (mean 38)</td>
<td>10/0/0</td>
<td>Cyberknife</td>
<td>1–24 (median 12)</td>
<td>0.47–9.8</td>
<td>57</td>
</tr>
<tr>
<td>Sahgal et al.[36], 2007</td>
<td>16/19</td>
<td>n.r.</td>
<td>14/5/0</td>
<td>Cyberknife</td>
<td>2–37 (median 25)</td>
<td>0.2–274.1</td>
<td>26</td>
</tr>
<tr>
<td>Selch et al.[37], 2009</td>
<td>20/25</td>
<td>17–78 (median 61)</td>
<td>25/0/0</td>
<td>Novalis</td>
<td>12–58 (median 18)</td>
<td>0.5–13.7</td>
<td>0</td>
</tr>
</tbody>
</table>

Target doses given in grays. Intra = Intradural primary tumor; extra = extradural primary tumor; n.r. = not recorded; LC = local control; OS = overall survival; PI = pain improvement; ME = meningioma; SC = schwannoma; NF = neurofibroma; regression tumor size = percentage of treated lesions with radiographic evidence of decrease in tumor size.
4 patients with sacral chordoma, 3 of which were not treated previously. Of these 3 patients, there was no evidence of local progression (30-month median follow-up) [36].

Although the early results of SR for benign nerve sheath tumors are promising, a longer follow-up is necessary in order to properly evaluate the efficacy of this technology. By nature, most of these tumors grow slowly, and there is no good study to demonstrate that the natural course or growth patterns of the tumors treated is altered by treatment. The cadence of relapse of acoustic neuromas may serve as a guide in this matter. For example, we have learned from our intracranial experience that the local progression rate after SR for acoustic neuromas in-

<table>
<thead>
<tr>
<th>Target dose/ isodose/fractions</th>
<th>Spinal cord dose limit</th>
<th>LC, %</th>
<th>OS, %</th>
<th>PI, %</th>
<th>Neurol. deficit, %</th>
<th>Improved neurol. deficit %</th>
<th>Major non-neurol. toxicity, %</th>
<th>Regression tumor size, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>15/100% (95% to PTV)</td>
<td>no prior RT: 12 Gy to 0.1 cm³; prior RT: 5 Gy to 0.5 cm³</td>
<td>95</td>
<td>25</td>
<td>43</td>
<td>0</td>
<td>n.r.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5–50.4/85–90%/1–28</td>
<td>2.4–42.8 Gy total dose</td>
<td>n.r.</td>
<td>97</td>
<td>94</td>
<td>3</td>
<td>n.r.</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>30/5 fractions or 27/3 fractions</td>
<td>&lt;10 Gy</td>
<td>84</td>
<td>70 at 1 year</td>
<td>1NU</td>
<td>n.r.</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>8–21/91%</td>
<td></td>
<td>56</td>
<td>71</td>
<td>50</td>
<td>n.r.</td>
<td>n.r.</td>
<td>n.r.</td>
<td>0</td>
</tr>
<tr>
<td>10–37.5/50–100%/1–5</td>
<td>2.2–27.1 Gy</td>
<td>100</td>
<td>59</td>
<td>97</td>
<td>21</td>
<td>n.r.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>12.5–25/80%</td>
<td>&lt;8 Gy to mean 0.6 cm</td>
<td>88</td>
<td>n.r.</td>
<td>86</td>
<td>0</td>
<td>n.r.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10–18/90%</td>
<td>&lt;10 Gy to 10% volume</td>
<td>n.r.</td>
<td>n.r.</td>
<td>85</td>
<td>n.r.</td>
<td>n.r.</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>24–45/90%</td>
<td>&lt;20 Gy point dose</td>
<td>95</td>
<td>65 at 1 year</td>
<td>81</td>
<td>5.5</td>
<td>42</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5.1–16/n.r./1–4</td>
<td>varied</td>
<td>87</td>
<td>66 at 1 year</td>
<td>97</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8–18/90%</td>
<td>&lt;10 Gy to 10% volume</td>
<td>n.r.</td>
<td>49 at 1 year</td>
<td>n.r.</td>
<td>1</td>
<td>n.r.</td>
<td>n.r.</td>
<td>n.r.</td>
</tr>
<tr>
<td>18–24/100%</td>
<td>12–14 Gy point dose</td>
<td>90</td>
<td>36 at 3 years</td>
<td>n.r.</td>
<td>0</td>
<td>n.r.</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
creased over the first 3 years after treatment [38]. Patients with neurofibromatosis may be predisposed to late progression of nerve sheath tumors after SR [39].

**SR for Intramedullary Spinal Cord Tumors**

Radiation therapy is commonly utilized in the treatment of spinal cord tumors, particularly as an adjuvant therapy in conjunction with surgical resection. Current microsurgical techniques allow for safe resection of tumors [28]. However, there is a population where radiosurgery could provide a benefit. Postoperative radiation therapy may play a role in reducing tumor recurrence and improving long-term survival in spinal cord ependymomas and astrocytomas [40, 41]. The role of radiation therapy, particularly SR, as a primary treatment modality is controversial. Ryu et al. [35] presented the largest series of intramedullary spinal tumors treated with SR. Seven hemangioblastomas and 3 ependymomas were treated. There was no evidence of tumor progression in any tumors, and 3 lesions decreased in size after SR [35].

**Conclusion**

The role of SR for tumors of the spine continues to be refined. Issues such as proper treatment dosage, spinal cord radiation tolerance, single-dose versus multi-dose SR continue to be investigated. However, despite the amazing accuracy and precision of our tools, we also have to acknowledge that the side effects can be devastating. Further refinements in hardware, software and techniques are still required.

The current literature provides support for SR as a primary treatment option for metastatic spine disease without evidence of spinal cord compression. SR may also play a role in the treatment of benign intradural tumors, particularly for patients who are poor candidates for definitive surgical resection. Evidence suggests that SR provides excellent local control and pain relief. Continued follow-up of these patients will help to elucidate the long-term outcomes of these patients.

**References**


