Skeletal metastases are a significant source of cancer-related morbidity and mortality, and although the exact incidence remains unknown, it is estimated that 350,000 individuals die with bone metastases annually in the US. Metastatic tumors of the spine are the most common malignancy of the spine, representing more than 90% of spinal tumor cases. It has been estimated that in 5%–10% of all cancer patients, metastatic disease to the spine develops during the course of the disease. Breast, prostate, and lung cancers account for 50%–85% of all bone metastases resulting in progressive pain, compression fractures, and spinal cord compression. As the axial skeleton, and specifically the spine, is the most common site of involvement, complications in these areas fre-

**Single-session and multisession CyberKnife radiosurgery for spine metastases—University of Pittsburgh and Georgetown University experience**

**Clinical article**

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**Object.** The authors compared the effectiveness of single-session (SS) and multisession (MS) stereotactic radiosurgery (SRS) for the treatment of spinal metastases.

**Methods.** The authors conducted a retrospective review of the clinical outcomes of 348 lesions in 228 patients treated with the CyberKnife radiosurgery at the University of Pittsburgh Cancer Institute and Georgetown University Medical Center. One hundred ninety-five lesions were treated using an SS treatment regimen (mean 16.3 Gy), whereas 153 lesions were treated using an MS approach (mean 20.6 Gy in 3 fractions, 23.8 Gy in 4 fractions, and 24.5 Gy in 5 fractions). The primary end point was pain control. Secondary end points included neurological deficit improvement, toxicity, local tumor control, need for retreatment, and overall survival.

**Results.** Pain control was significantly improved in the SS group (SSG) for all measured time points up to 1 year posttreatment (100% vs 88%, p = 0.003). Rates of toxicity and neurological deficit improvement were not statistically different. Local tumor control was significantly better in the MS group (MSG) up to 2 years posttreatment (96% vs 70%, p = 0.001). Similarly, the need for retreatment was significantly lower in the MSG (1% vs 13%, p < 0.001).

**Conclusions.** Single-session and MS SRS regimens are both effective in the treatment of spinal metastases. While an SS approach provides greater early pain control and equivalent toxicity, an MS approach achieves greater tumor control and less need for retreatment in long-term survivors.

**Key Words** • radiosurgery • spinal metastasis • outcome • repeat irradiation • oncology
quent lead to significant impact on the quality of life of patients with cancer, the cost of which is frequently underreported.4 Palliation of pain, reversing neurological symptoms, and spinal cord compression relief are the primary goals in the treatment of patients with spinal metastases.17

Management strategies are often directed by patients’ clinical presentation and may include EBRT, chemotherapy, analgesics, open surgical decompression with or without stabilization, and percutaneous cement augmentation. For metastatic cord compression, surgical intervention has an important role. Patchell and colleagues20 demonstrated that direct decompressive surgery followed by radiation therapy is superior to radiation alone for patients with spinal cord compression. This approach improved ambulatory rates, opioid requirements, and survival. Additionally, for spinal instability, surgery is the only treatment modality that can provide stabilization and immediate decompression. Refinement of the combination of a number of these strategies has improved clinical outcome and the quality of life of many patients, although as many as 50% of patients will require further intervention for recurrent pain.7,14

External-beam radiation therapy remains the mainstay of adjuvant therapy for spinal metastases and offers significant short-term and, in some instances, long-term palliation. Although 30 Gy in 10 fractions is the most common fractionation schedule, multiple fractionation schemes have been reported.24 This fact reflects the heterogeneity in the patient population and tumor histology. Conventional radiotherapy typically alleviates pain in 57%–63% of patients.1,15,21 However, there are certain disadvantages to this approach, the most notable of which is the irradiation of surrounding critical and uninvolved normal tissues. These characteristics make it difficult to deliver large, precisely targeted doses to the spine while protecting critical structures such as the spinal cord. Thus, over the past decade, support for treating spinal metastases with SRS has grown, either as primary palliation or as salvage therapy after the failure of the prior radiotherapy or surgery. Stereotactic radiosurgery can deliver a highly conformal, large radiation dose to a localized tumor while sparing the adjacent spinal cord, thereby reducing the risk of radiation-induced myelitis.5,10,12

Overall, spine SRS delivery is generally classified into 2 groups based on treatment technology: CyberKnife radiosurgery (Accuray, Inc.) and multileaf collimator LINAC platforms. Dosimetric comparisons between the CyberKnife and LINAC multileaf collimator systems are limited but appear to demonstrate that both are effective in creating adequately complex treatment plans for spinal SRS.25 Researchers at Stanford University Hospital were the first to publish their experience using SRS to treat spinal metastases with the CyberKnife system.18 Their study demonstrated that CyberKnife could deliver therapeutic doses to the spine while markedly limiting the dose to the nearby critical structures. Since the publication of that report, several other centers have evaluated the CyberKnife and other technologies for the treatment of spinal metastases with promising results.5,8–12,25,27

At the GUMC, Degen et al.7 have reported on the treatment of 51 patients with 72 spinal tumors. Lesions received a mean dose of 21.2 Gy over a mean of 3.6 fractions. The authors found that nearly all patients reported significant improvement in pain and quality-of-life scores during the 1-year follow-up. Additionally, there were few reportable adverse events. The majority of patients (52.8%) had previously undergone EBRT. Of the patients who had previously received EBRT, 16% had local recurrences after SRS. However, in the patients who had not previously undergone EBRT, tumor control was 100%. Nelson et al.19 analyzed 33 lesions in 32 patients in whom they used a mean of 3 fractions (range 1–4 fractions) of 7 Gy per fraction (range 5–16 Gy); 40.6% of patients had complete pain relief and 53.1% had partial relief in 1 month.

The largest CyberKnife study for spinal metastases to date was reported by investigators at the UPCI who used a single-fraction approach.15 Three hundred ninety-three patients with 500 spinal lesions received a mean of 20 Gy (range 12.5–25 Gy). Long-term pain improvement was observed in 86% of patients at a median follow-up of 21 months, and long-term tumor control was achieved in 90% of the cases. Ryu et al.23 have also reported on 177 patients who underwent SS SRS in which the Novalis System was used with doses from 8 to 18 Gy. Pain relief was achieved in 85% of the patients. Benzil et al.2 reported on 31 patients who underwent single-fraction (range 6–8 Gy) SRS, and pain relief was achieved for 94% of tumors.

While these studies and others have demonstrated success in treating spinal metastases with SRS, the ideal dose and other treatment parameters have yet to be determined because, in the described studies, each institution has used different treatment parameters. For example, the UPCI used a regimen of 16–21 Gy delivered in a single fraction for the majority of patients.5–12 This contrasts with the approach devised at GUMC,2,6 in which 21–37 Gy were delivered in 1–5 fractions (median 3 fractions). Stanford University also used a fractionated regimen, yet administered a single fraction whenever feasible.13 This variability in fraction number, total dose, and patient selection criteria warrants an evaluation of the best approach based on each patient’s disease characteristics, location, and histology among other factors.

This is the first study to compare the efficacy of MS and SS SRS treatments in terms of controlling pain, neurological deficits, toxicity, and recurrence of tumor in a population of patients with spinal metastases.

Methods

This study involved the retrospective review of the treatment records of 348 metastatic lesions to the spine in 228 consecutive patients treated at GUMC and the UPCI between January 2000 and 2008. This study was conducted under a formal institutional review board–approved protocol. Eligible patients had a primary diagnosis of melanoma, lung, renal cell, breast, colon, prostate, multiple myeloma, or thyroid cancer metastatic to the spine. Patients diagnosed with spinal metastatic lesion(s) at all levels were included in the study. Patients with or without history of radiation treatment or surgery for the same lesion were also included. We excluded patients with spinal compression.
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instability, life expectancy less than 3 months, or frank cord compression (defined as a metastatic lesion with central canal extension and impact on the cord with no gap between the cord and the epidural lesion).

Tumors were treated with either an MS (n = 153 lesions) or SS (n = 195 lesions) SRS treatment regimen. Patients at UPCI primarily were treated with an SS approach and those at GUMC with an MS approach, as per the treatment algorithms and practice patterns independently devised at each institution.

Data regarding sex, age, treatment history, primary cancer pathology, and history of spinal metastases were collected. The primary end point was pain relief. Secondary end points included local tumor control, median survival time, treatment toxicity, and neurological improvement. Local control was assessed based on CT or MRI studies 6 months posttreatment. Additionally, data were collected for outcome assessment at regular intervals up to 2 years. Toxicity was assessed using the National Cancer Institute’s Common Toxicity Criteria (version 3).

Pretreatment Assessment

Each patient was evaluated by a multidisciplinary team consisting of a neurosurgeon, radiation oncologist, imaging specialist, and, when indicated, a pain specialist and a social worker. Pretreatment CT, MRI, and prior radiation records were used in formulating treatment. In general, patients were simulated in the supine, feet-first position for CyberKnife robotic radiosurgery. In a subset of patients treated before 2004, including patients in both the MS and SS cohorts, gold fiducial markers were placed in or around the spine to enable near-real time tracking. After 2004, some patients were treated with the CyberKnife tracking software, Xsight Spine Tracking System (Accuray), which eliminated the need for surgical implantation of fiducial markers. The Xsight system registers unique nonrigid and bony anatomical landmarks to track, detect, and correct for movement of the spine in real time during treatment. The details of this frameless radiosurgical system have been described.

Treatment Planning

In each case, the radiosurgical treatment plan was designed based on the tumor’s geometry, proximity to the spinal cord, and location. The gross tumor volume was the tumor discernible on the relevant imaging study (CT scan with contrast or MR image). The clinical treatment volume included the gross tumor volume and a margin of tissue at risk for microscopic extension determined by the neurosurgeon at the time of target delineation. The planning target volume was equal to the clinical treatment volume. The spinal cord, cauda equina, nerve roots, and bowels were contoured as critical structures. Treatment planning was conducted on the CT scan; however, a fused CT-MR image was consulted whenever further visualization was necessary. An inverse treatment planning method, along with a linear optimization algorithm, was used. The target volume was designed to include the entire vertebral body and/or soft-tissue component at the respective spinal level.

Treatment Delivery

The process of treatment delivery has been described in detail previously. Briefly, the patients were positioned supine on the CyberKnife treatment couch with the appropriate immobilization aides, Aquaplast mask for cervical lesions, or conformable alpha cradle for thoracic, lumbar, or sacral lesions. Patients receiving 3–5 fractions were treated daily. Patients were offered a mild sedative when one was considered helpful by the treating physician.

Patient Evaluations

Study coordinators at each institution extracted the data from medical charts and other sources (for example, CT and MR images/reports) and exported them into a database for biostatistical analysis. Outcomes were assessed based on pain level, neurological symptoms, local tumor control, toxicity, overall survival, and need for retreatment.

Pain. The radiosurgical team assessed patient-reported pain relief. Patients were instructed to evaluate pain as improved, stable, or worse compared with their baseline, pretreatment pain level. Patients at both institutions were asked to evaluate pain using this same relative scale. Data were collected at Weeks 1–2 and at Months 2–3, 4–6, 7–12, and 12–24 after treatment.

Neurological Assessment. Neurological status was evaluated for patients who presented with neurological deficits at baseline. Neurological deficits, including paresis and paresthesias, attributable to the treated lesion were assessed and followed by the radiosurgical team. Patients at both institutions were asked to compare any neurological deficit with baseline, pretreatment level and rate it as improved, stable, or worse. Data were collected at Weeks 1–2 and at Months 2–3, 4–6, 7–12, and 12–24 after treatment.

Local Control. Local tumor control was evaluated based on CT/MR images, comparing status before and after treatment. The images were reviewed and assessed by the radiosurgical team. Tumor growth less than 25% was classified as “local control.”

Toxicity. Adverse events were assessed using the National Cancer Institute’s Common Toxicity Criteria (version 3). Information on the type of the adverse event, including start date, stop date, treatments received, relationship to the radiosurgery treatment, outcome, need for hospitalization, and seriousness, was collected.

Retreatment. Rates of retreatment were assessed based on whether the patient had received previous CyberKnife SRS to the same or an overlapping lesion.

Statistical Analysis

The study was powered to detect a greater than 15% difference in pain relief rate, with an α of 0.05. Based on the actual sample size, the study has a statistical power of 83.21%. Data analysis was performed using SAS version 9.1.
9.2 and supplied by STATA version IE10 and PASS 2008. Chi-square tests were used for testing the difference between categorical variables with adequate sample size in each category (≥5), Fisher exact test for the categorical variables with inadequate sample size (<5), and Student t-tests for continuous variables. An α significance level of 0.05 was chosen, and a p value < 0.05 was considered statistically significant. Kaplan-Meier curves were calculated from the survival data. We defined BED as nd (1 + d/α/β), where n is the number of fractions, d is the daily dose, units were in Gray, and the assumed α/β ratio was 10. Multinomial logistic models were used to control for 2 potential confounding variables: BED and initial tumor volume. Probability values were reported separately for each pairwise comparison.

**Results**

**Patient Characteristics**

With a median follow-up period of 360 days for the entire cohort (MSG 360 days and SSG 360 days), the study retrospectively evaluated 348 spinal lesions in 228 patients (MSG 153 lesions and SSG 195 lesions). In the MSG (n = 104), there were 55 women and 49 men with a mean age of 59 years (range 18–83 years). This was comparable to the SSG (n = 124), in which there were 63 women and 61 men with a mean age of 59 years (range 31–85 years). Patients in the MSG were more likely to receive SRS as primary therapy than those in the MSG (36% and 5%, respectively; p < 0.001).

Among all patients, 27% had prior surgical management of the metastatic lesion prior to irradiation, and there was no intergroup difference. However, patients in the SSG were more likely to undergo SRS as primary therapy than those in the MSG (36% and 5%, respectively; p < 0.001).

**Treatment Characteristics**

The mean prescription dose in the MSG was 20.6 Gy delivered in 3 fractions (range 9.0–26.3 Gy), 23.8 Gy in 4 fractions (range 16.0–18.0 Gy), and 24.5 Gy in 5 fractions (range 15.0–35.0 Gy), most commonly prescribed to the 72% isodose line (range 50%–85%). In the SSG, the mean prescription dose was 16.3 Gy (range 6.0–20.0 Gy) prescribed to the 80% isodose line (range 70%–95%). Because the spinal cord, its nerve roots, and cauda equina were the key critical structures in virtually all cases, special care was used in the design of all radiosurgical plans. The mean maximum dose to the spinal cord was 11.8 Gy for 3 fractions, 10.6 Gy for 4 fractions, and 15.6 Gy for 5 fractions in the MSG, whereas it was 10.2 Gy in the SSG. Because treatments were delivered in a variable number of fractions, the relative BED in the SSG compared with that in the MSG had to be taken into account. The mean BED prescription dose, for an α/β ratio of 10, in the SSG was significantly greater than that in the MSG (43.2 vs 35.7 Gy, respectively; p < 0.001).

**Clinical Outcomes**

**Pain.** More than 96% of patients presented with pain as their primary indication for SRS (98% and 96%, respectively; p < 0.01). The primary indication was pain in both the MSG and SSG (98% and 96%, respectively). In the MS arm, 38% of patients had neurological symptoms at baseline in contradistinction to the SS arm, in which only 9% of patients reported having such symptoms (p < 0.001). Patients in the SSG were more likely to receive SRS as primary therapy than those in the MSG (36% and 5%, respectively; p < 0.001).

**TABLE 1: Characteristics of the treatment group at baseline**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Radiosurgical Treatment (%)</th>
<th>MSG</th>
<th>SSG</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>previous EBRT</td>
<td>57 55</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>prior op to treat lesion</td>
<td>26 28</td>
<td>0.676</td>
<td></td>
<td></td>
</tr>
<tr>
<td>primary treatment modality</td>
<td>5 36</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>primary indications for SRS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pain</td>
<td>98 96</td>
<td>0.522</td>
<td></td>
<td></td>
</tr>
<tr>
<td>neurological deficit</td>
<td>38 9</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>spinal cord compression</td>
<td>18 4</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bone erosion</td>
<td>33 1</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>levels treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cervical</td>
<td>9 10</td>
<td>0.966</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cervicothoracic</td>
<td>7 2</td>
<td>0.006*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>thoracic</td>
<td>52 47</td>
<td>0.352</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lumbar</td>
<td>19 31</td>
<td>0.012*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sacral</td>
<td>12 11</td>
<td>0.762</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lesion vol (cm³)</td>
<td>81 35</td>
<td>&lt;0.001*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>0.173–486</td>
<td>0.1–257</td>
<td></td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>12–31.1</td>
<td>3.7–22.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant (p < 0.05).

**TABLE 2: Lesion histological types**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Radiosurgical Treatment (%)</th>
<th>MSG</th>
<th>SSG</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>renal cell</td>
<td>9 20</td>
<td>0.005*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>breast</td>
<td>27 24</td>
<td>0.477</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lung</td>
<td>17 19</td>
<td>0.634</td>
<td></td>
<td></td>
</tr>
<tr>
<td>melanoma</td>
<td>4 10</td>
<td>0.026*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>colorectal</td>
<td>5 5</td>
<td>0.792</td>
<td></td>
<td></td>
</tr>
<tr>
<td>prostate</td>
<td>7 5</td>
<td>0.306</td>
<td></td>
<td></td>
</tr>
<tr>
<td>multiple myeloma</td>
<td>1 1</td>
<td>&gt;0.999</td>
<td></td>
<td></td>
</tr>
<tr>
<td>thyroid</td>
<td>10 6</td>
<td>0.206</td>
<td></td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>19 10</td>
<td>0.021*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant (p < 0.05).
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their primary symptom. The long-term treatment response was evaluated (Table 3). As depicted in Table 3, pain relief, defined as a long-term decrease in pain measured after 4–6 months, was not significantly different between the groups (73% [MSG] vs 71% [SSG], p = 0.617). However, pain control, defined as the percentage of patients either pain relief or stabilization of pain was achieved, was significantly higher in the SSG than the SSG for all measured time points up to 12 months (100% and 88%, respectively; p = 0.003). At 12 months, pain had improved in 71% of the SSG patients and stabilized in the other 29%. At this time point in the MSG, pain improvement was achieved in 70% of patients, stabilization of pain was achieved in 18%, and pain had worsened in 12% (Fig. 1). The statistically greater pain response observed in the SSG persisted even after corrections were made for this group’s larger BED.

Neurological Status. In the MSG, 38% of patients presented with neurological deficits compared with 9% in the SS cohort. Spinal cord compression was present in 18% in the MSG and in 4% in the SSG (p < 0.001). Patients in the MSG and SSG were equally likely to experience improved neurological function at each evaluation time point up to 2 years. At the 1- to 2-year time point, 71% of patients in the SSG and 79% of those in the MSG had improved neurological symptoms. The remaining patients had stabilized symptoms; no patients in either group were found to have progression of neurological symptoms. This remained the case when BED was taken into account.

Tumor Control. Tumor control in both cohorts was evaluated at the key time points summarized in Fig. 2. Control was assessed based on CT, MRI, or a combination. At 2, 4, 6, 12, and 24 months, tumor control was superior in the MSG. At 2 years, tumor control probability in the MSG was 96% compared with 70% in the SSG (p = 0.001). The greater tumor control observed in the MSG remained significant when the initial volume of the tumor was adjusted for both groups.

**TABLE 3: Summary of pain and radiological outcome for the 4 most prevalent histological tumor types**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MSG</th>
<th>SSG</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>long-term pain improvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all patients</td>
<td>73</td>
<td>71</td>
<td>0.617</td>
</tr>
<tr>
<td>renal cell</td>
<td>63</td>
<td>82</td>
<td>0.378</td>
</tr>
<tr>
<td>breast</td>
<td>72</td>
<td>61</td>
<td>0.51</td>
</tr>
<tr>
<td>lung</td>
<td>76</td>
<td>50</td>
<td>0.125</td>
</tr>
<tr>
<td>melanoma</td>
<td>100</td>
<td>55</td>
<td>0.119</td>
</tr>
<tr>
<td>long-term radiological control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all patients</td>
<td>89</td>
<td>61</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>renal cell</td>
<td>67</td>
<td>88</td>
<td>0.528</td>
</tr>
<tr>
<td>breast</td>
<td>96</td>
<td>83</td>
<td>0.219</td>
</tr>
<tr>
<td>lung</td>
<td>88</td>
<td>0</td>
<td>0.010*</td>
</tr>
<tr>
<td>melanoma</td>
<td>100</td>
<td>50</td>
<td>0.182</td>
</tr>
</tbody>
</table>

* Statistically significant (p < 0.05).

**Fig. 1.** Pain control in the treatment groups. Pain control, defined as the sum of the percentage of patients with decreased and stable pain, is greater in the SSG. These results are statistically significant at each time point (p < 0.05).

**Fig. 2.** Radiographic tumor control in the treatment groups. Tumor control, defined as the sum of the percentage of tumors that decreased in size and the percentage that did not grow, was better in the MSG. These results were statistically significant at each time point (p < 0.05).

**Toxicity Assessment.** Treatment-related toxicity was assessed for the entire cohort. The overall rate of any adverse event was similar in both groups (4.6% in SSG and 5.9% in MSG). There was one Grade III complication in the SSG, but no Grade II or III complications in the MSG. The severity of the adverse events was not statistically different between the groups.

**Retreatment.** The need for retreatment is an important assessment parameter of the overall durability of SRS. In the SSG, 13% of patients required retreatment with radiosurgery compared with 1% in the MSG (p < 0.001).

**Survival.** Median overall survival for the entire cohort was 13 months (11 months in the SSG and 18 months in the MSG). In the SSG, the 1-year overall survival was 46%, whereas in the MSG it was 63% (p = 0.002).

**Discussion**

In this retrospective study comparing outcomes between SS and MS SRS for spinal metastases, we found the former resulted in significantly better pain control and no differences in adverse events or improvement in neu-
rological deficits. External-beam radiation therapy has long been considered the appropriate first-line treatment for metastatic tumors of the spine.\textsuperscript{1,15,21} In the setting of spinal instability or cord compression, however, surgery followed by radiation therapy has been shown to produce superior functional outcomes and survival than radiation therapy alone.\textsuperscript{20}

Over the past decade, there has been increasing support to use SRS for treating patients who have undergone spinal radiation therapy or have undergone radiation therapy that failed. The rationale for using SRS instead of EBRT is the former’s ability to deliver larger doses with greater precision while sparing the spinal cord, as depicted in Fig. 3. Over the past 10 years, several large institutions, including UPCI and GUMC, have reported their success treating these lesions with SRS. However, the ideal fractionation schemes for SRS remain a relative unknown, and both institutions employ different pathways for managing such patients.

This study provides evidence that both fractionation schemes demonstrate long-term pain improvement in the majority of patients. The SSG was found to have a higher long-term pain control rate as a result of a greater number of patients reporting stabilized pain and no patients reporting worsened pain. No intergroup differences were noted in the neurological improvement, and complication rates were also not statistically different. Radiographically, local tumor control was significantly better in the MSG. Furthermore, the retreatment rate was significantly higher in the SSG. Finally, 1-year survival was significantly greater in the MSG and should be considered in patients who have a relatively long life expectancy.

It is important to emphasize that there was no statistically significant difference in complications between the groups. There was one Grade III complication (0.5%) in the SSG but no Grade III complications in the MSG. Although the maximum dose to the spinal cord was greater in the MSG (12.6 Gy in the MSG vs 10.2 Gy in the SSG, \(p < 0.001\)), a weighted comparison of the doses using the linear quadratic formalism of Fowler revealed a larger BED in the SSG. The calculated BED (using an \(\alpha/\beta\) ratio of 2.2 for the spinal cord) demonstrated that the maximum dose impact to the spinal cord was greater in the SSG than in the MSG (57.5 and 30.9 Gy, respectively).

When SRS fails to achieve long-term local tumor control, patients may require costly further interventions, including additional radiation, surgery, chemotherapy, or a combination thereof. This can lead to increased morbidity and healthcare expenditures. In our series, MSG patients had significantly higher rates of tumor control than SSG patients (96\% vs 70\%, respectively) at all time points up to 2 years after treatment. Furthermore, retreat-
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ment rates were significantly lower in MSG patients than in SSG patients (1% vs 13%, respectively). The significant difference in local control rates was not found to be related to the initial tumor volume.

We observed a statistically significant increase in 1-year survival in MSG patients (63%) compared with SSG patients (46%), despite the larger overall mean size of the tumors treated with MS SRS and despite the smaller calculated BED in the MSG. This difference was in part the result of the greater efficacy of treatment of melanomas in the MSG (100% treatment efficacy at 12 months), compounded with the greater number of melanomas in the SSG, in which treatment efficacy was only 55%.

The present study does have a number of limitations. As a retrospective series, many of differences between the 2 groups, including tumor histology, presenting neurological symptoms, and other variables, could not be controlled. Certainly the fact that the 2 study groups did have some differences in histology must be noted; however, it is interesting that, despite the increased number of particularly radioresistant tumors (including renal cell carcinoma and melanoma) in the SSG, the patients in this group still experienced significantly better pain control. In addition, in this study we adjusted for differing fractionation schedules by calculating BED using an assumed α/β ratio of 10. We recognize different histological types will have varying ratios, but a value of 10 was assumed for the purposes of this calculation. Finally, there was variability in the patients who were referred for surgery over the course of study between 2000 and 2008. In 2005, Patchell and colleagues20 published a landmark series demonstrating the role for surgery followed by radiation therapy in the setting of spinal cord compression. Certainly for cases managed after 2005, surgical intervention was routinely attempted when possible, but in the earlier experience surgery may not have been used routinely.

This study’s strengths lie in the extensive experience with radiosurgery in both institutions as evidenced by large patient population. Furthermore, the study sheds light on the outcomes of patients treated with differing SRS schedules, an important question for which continued investigation is necessary. While this retrospective series alone may not provide sufficient evidence to recommend one fractionation schedule over another, the present retrospective series does demonstrate that both approaches appear to be efficacious in controlling pain. The ongoing Radiation Therapy Oncology Group (RTOG 0631) study is a prospective, randomized trial comparing SRS (16 or 18 Gy in 1 fraction) to EBRT (8 Gy in 1 fraction) for spine metastases. This RTOG study and future studies that may compare various SRS fractionation schemes will continue to help elucidate the role and dose of SRS for spinal metastases.

Conclusions

Single-session and MS SRS is safe and effective in treating spinal metastases. Over the 1st year, pain control was superior with SS treatment compared with MS treatment. There was no statistically significant difference in toxicity between treatment groups. Multisession treat-

ment achieved greater long-term tumor control and fewer relapses requiring local retreatment.

Disclosure

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