Prognostic factors associated with pain palliation after spine stereotactic body radiation therapy

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OBJECT The number of patients with spinal tumors is rapidly increasing; spinal metastases develop in more than 30% of cancer patients during the course of their illness. Such lesions can significantly decrease quality of life, often necessitating treatment. Stereotactic radiosurgery has effectively achieved local control and symptomatic relief for these patients. The authors determined prognostic factors that predicted pain palliation and report overall institutional outcomes after spine stereotactic body radiation therapy (SBRT).

METHODS Records of patients who had undergone treatment with SBRT for either primary spinal tumors or spinal metastases from June 2008 through June 2013 were retrospectively reviewed. Data were collected at the initial visit just before treatment and at 1-, 3-, 6-, and 12-month follow-up visits. Collected clinical data included Karnofsky Performance Scale scores, pain status, presence of neurological deficits, and prior radiation exposure at the level of interest. Radiation treatment plan parameters (dose, fractionation, and target coverage) were recorded. To determine the initial extent of epidural spinal cord compression (ESCC), the authors retrospectively reviewed MR images, assessed spinal instability according to the Bilsky scale, and evaluated lesion progression after treatment.

RESULTS The study included 99 patients (mean age 60.4 years). The median survival time was 9.1 months (95% CI 6.9–17.2 months). Significant decreases in the proportion of patients reporting pain were observed at 3 months ($p < 0.0001$), 6 months ($p = 0.0002$), and 12 months ($p = 0.0019$) after treatment. Significant decreases in the number of patients reporting pain were also observed at the last follow-up visit ($p = 0.00020$) (median follow-up time 6.1 months, range 1.0–56.6 months). Univariate analyses revealed that significant predictors of persistent pain after intervention were initial ESCC grade, stratified by a Bilsky grade of 1c ($p = 0.0058$); initial American Spinal Injury Association grade of D ($p = 0.011$); initial Karnofsky Performance Scale score, stratified by a score of 80 ($p = 0.002$); the presence of multiple treated lesions ($p = 0.044$); and prior radiation at the site of interest ($p < 0.0001$). However, when multivariate analyses were performed on all variables with p values less than 0.05, the only predictor of pain at last follow-up visit was a prior history of radiation at the site of interest ($p = 0.0038$), although initial ESCC grade trended toward significance ($p = 0.073$). Using pain outcomes at 3 months, at this follow-up time point, pain could be predicted by receipt of radiation above a threshold biologically effective dose of 66.7 Gy.

CONCLUSIONS Pain palliation occurs as early as 3 months after treatment; significant differences in pain reporting are also observed at 6 and 12 months. Pain palliation is limited for patients with spinal tumors with epidural extension that deforms the cord and for patients who have previously received radiation to the same site. Further investigation into the optimal dose and fractionation schedule are needed, but improved outcomes were observed in patients who received radiation at a biologically effective dose (with an α/β of 3.0) of 66.7 Gy or higher.

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KEY WORDS stereotactic; radiotherapy; SBRT; oncology; pain palliation

ABBREVIATIONS ASIA = American Spinal Injury Association; BED = biologically effective dose; ECOG = Eastern Cooperative Oncology Group; ESCC = epidural spinal cord compression; KPS = Karnofsky Performance Scale; SBRT = stereotactic body radiation therapy.

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THE number of patients with spinal tumors of either primary or metastatic origin is rapidly increasing; spinal metastases develop in more than 30% of cancer patients during the course of their illness.^{28,41} In this patient population, spinal lesions are a common source of decreased quality of life, secondary to increased bone pain or frank epidural spinal cord compression (ESCC) that can result in permanent neurological deficits.^{17,19,29} Although symptoms are managed with steroid and/or analgesic use, progressive tumor growth often necessitates local therapy.

Surgical decompression and/or stabilization is the standard of care for patients with malignant epidural spinal cord compression from solid tumors or tumors resistant to conventional external-beam radiation.^{29,38} External-beam therapy represents an alternative noninvasive technique that has historically been performed in patients who are not considered surgical candidates because of poor performance status, extensive systemic disease, or concurrent medical conditions or in patients who have radiosensitive tumors, such as hematological malignancies. Unfortunately, control rates after conventional radiation therapy are not ideal for most solid tumors because the radiation dose must be limited to respect the tolerance of the spinal cord and other adjacent structures.¹¹

Recently, spine stereotactic body radiation therapy (SBRT) has been used to precisely deliver radiation, allowing for dose escalation and improved local control while limiting the dose to the adjacent normal structures and spinal cord.^{1,4,12,15,16,25,32,33} A recent meta-analysis reported a local control rate of 92% and symptomatic relief for 82% of patients.²⁰

Although spine SBRT is accepted as a safe and effective noninvasive treatment alternative for spinal metastases, many questions remain. For example, although spine SBRT is generally accepted for patients with oligometastatic disease, its role for patients with advanced disease is controversial. Similarly, the optimal dose and fractionation schedule remain uncertain. The purpose of this study was to review outcomes in a heterogeneous cohort of patients with advanced metastatic disease treated with spine SBRT at a single institution. Our intent was to determine prognostic factors that predicted pain palliation and to report overall institutional outcomes.

Methods

Records of patients who underwent spine SBRT for either primary spinal tumors or spinal metastases from June 2008 through June 2013 were retrospectively reviewed. Patients were excluded if they received treatment for intramedullary lesions. All patients had undergone initial evaluation that included a neurological exam, pain assessment, and imaging confirmation of a spinal lesion.

Data Collection

Details recorded from the medical record reviews were general demographics, oncological history, treatment history, clinician assessments, and medication use. Disease location was confirmed via cross-referencing MR images, CT images, and radiographs with radiologist-written notes. The radiation treatment plan parameters of dose, fractionation, and target coverage were also recorded. Ra-

diation fractionation schemes were converted to biologically effective doses (BEDs) with an α/β of 3.0.

Functional status was assessed by using the Karnofsky Performance Scale (KPS). For most patients, either a KPS score or an Eastern Cooperative Oncology Group (ECOG) score was provided by the oncologist responsible for patient assessment before SBRT. When only an ECOG score was provided, ECOG scores were converted to KPS scores by using pertinent clinical patient information and the following approximate conversion, which has been validated in a large sample of lung cancer patients: ECOG scores of 0–1, 2, and 3–4 are roughly equivalent to KPS scores of 80–100, 60–70, and 10–50, respectively.⁷ For patients for whom neither ECOG nor KPS scores were provided, an estimate was obtained from clinical records, particularly clinician-acquired social histories that determined the extent of functional independence exhibited by the patient in question. For these patients, functional status was retrospectively evaluated independently by 2 evaluators, and the final KPS score was reported as the average of these 2 scores.

The primary outcome was the presence of pain corresponding with the spine radiosurgery target. Pain was scored in a binary fashion. In terms of determining improvement in pain, successful pain treatment was defined as patient-reported complete remission of previous pain at the treatment level, a pain score of 0, or recurrent pain that could no longer be attributable to the lesion of interest. Initial use of narcotics, another measure of pain, was recorded as the prescription of narcotics, either as needed or scheduled. Neurological status was assessed by using the American Spinal Injury Association (ASIA) Impairment Scale, which assigns patients with spinal lesions to letter categories from A (total loss of neurological function below the level of interest) to E (absence of functional deficits). For this study, patients who were evaluated as having 5/5 strength in all pertinent muscle groups as well as intact sensation and touch were deemed to have ASIA Grade E status. Neurological status was assigned only if performance of a neurological examination by a board-certified neurologist, radiation oncologist, or neurosurgeon was documented. These parameters were assessed at approximately 1, 3, 6, and 12 months and at the last documented clinical visit.

When medical records were incomplete, survival time was determined by using the Social Security Death Index Master File. For patients lost to follow-up and for whom death was not noted in the Social Security Death Index Master File, dates corresponding to the last clinical visit were used as last follow-up.

Imaging

One board-certified neuroradiologist (N.A.) assessed the extent of ESCC in all cervical and thoracic lesions by reviewing available images taken before SBRT. ESCC was evaluated according to the 6-point scale popularized by Bilsky et al. in 2010.³ This scale relies on the use of axial T2-weighted MR images to judge the extent of extraosseous tumor growth and thecal sac compression. The 6 grades (0, 1a, 1b, 1c, 2, and 3) were assigned as follows: Grade 0 indicates disease that is contained in a vertebral

body without any epidural impingement; Grade 1 indicates disease that extends outside of the vertebral body with subarachnoid space impingement in the absence of spinal cord deformation; Grade 2 indicates disease with epidural extension that partially deforms the spinal cord without completely obliterating the subarachnoid space; and Grade 3 indicates spinal cord deformation such that no CSF is visible at the level of interest. Grade 1 was further subdivided into 1a (epidural impingement without deformation of the thecal sac, 1b (epidural impingement with deformation of the thecal sac but without spinal cord abutment), and 1c (deformation of the thecal sac with spinal cord abutment). For the purposes of analysis, for patients with multiple cervical and/or thoracic lesions, we considered tabulated ESCC values to correspond with the highest such value among the lesions. For example, for a patient with a T-5 ESCC of Grade 1b and a T-10 ESCC of Grade 2, a value of 2 was tabulated.

Lesions that had been appropriately followed up with MRI were further analyzed for evidence of local progression. Local progression was assessed by the presence of either progressive canal narrowing on serial MR images or evidence of tumor growth. If results of a single scanning session were indeterminate, serial scanning was used to determine tumor growth. The date of progression was backdated to the date of the first indeterminate scan. Additional radiographic analysis included serial detection of compression fractures, before and after radiosurgery. This latter analysis was limited to patients who did not undergo additional decompressive surgery. Data pertaining to treatment with vertebroplasty or kyphoplasty were also acquired.

Statistical Analysis

Overall survival times after SBRT were assessed by using Kaplan-Meier estimates. The McNemar test was used to determine significant changes in the proportion of patients experiencing pain at each time point compared with that at initial presentation. The logistic regression model was used to assess determinants of eventual treatment failure at the 3-month time point, as assessed by presence of pain. Odds ratios and 95% confidence intervals were also computed by using this method. Fitted values of pain at the 3-month time point obtained from the logistic regression analysis of radiation doses were used to obtain a threshold radiation dose that predicted treatment success. Statistical analyses were performed by using STATA 11.0 (StataCorp, LP) and R version 3.0.2 (R Core Team). Significance was established when comparisons resulted in probability values less than or equal to 0.05.

Results

Demographics and Initial Clinical Presentation

A total of 99 patients (mean age 60.4 years) were included in this study. Tumor information is provided in Table 1. Patient demographics and initial clinical presentation information are summarized in Table 2. At the time of SBRT, 47 patients had concomitant metastases of the brain, liver, lung, or kidney, and 51 had extraspinal osseous metastases.

TABLE 1. Tumor locations and histological types

Characteristic	No. of Lesions/Patients
Tumor location	
Cervical	22
Thoracic	60
Lumbar	43
Sacrum	5
Coccyx	1
Total	131
Histological type	
Renal cell carcinoma	18
Breast	12
Prostate	10
Non-small cell lung carcinoma	8
Sarcoma	7
Colon	6
Chordoma	5
Melanoma	4
Nasopharyngeal	4
Pancreas	3
Urothelial	3
Atypical pulmonary carcinoid	3
Other	16
Total	99

At the time of presentation, 79 patients reported pain and 49 reported use of narcotics, on either an as-needed or daily-dose basis. A total of 73 were classified as ASIA Grade E, with no motor or sensory deficits. For 60 patients, bony cervical or thoracic lesions were present and initial T2-weighted MR images were available for review; most (51.7%) of these patients exhibited disease that did not contact the spinal cord, garnering a Bilsky grade of 0, 1a, or 1b. The patient with Bilsky Grade 3 disease underwent concomitant surgical decompression.

Survival Times

The median survival time for the overall cohort was 9.1 months (95% CI 6.9–17.2 months) (Fig. 1). The percentage of patients who survived 1 year was 43.7%.

Pain Improvement

The proportion of patients who reported local pain at the site of treatment consistently declined from initial presentation to 6 months after SBRT (Fig. 2). However, the proportion who reported local pain increased slightly at 12 months. Narcotic use exhibited a similar trend, although the proportion of patients taking a daily dose of narcotics was lower at 12 months than at any previous time point. When follow-up information was available at a given time point, it was compared with initial presentation information for the same patients. Significant decreases in the proportion of patients reporting pain were observed at 3 months ($p < 0.0001$), 6 months ($p = 0.0002$), and 12 months ($p = 0.0019$) after treatment. Significant

TABLE 2. Characteristics of 99 patients

Characteristic/Category	Total
Mean age (SD)	60.4 (12.1)
Sex	
M	51
F	48
Initial pain	
No	20
Yes	79
Initial narcotic use*	
No	50
Yes	49
Initial ASIA grade	
D	26
E	73
Initial ESCC score	
0	13
1a	6
1b	12
1c	6
2	22
3	1
Total	60
Initial KPS score	
80–100	67
50–70	31
0–40	1
Decompressive surgery	
No	67
Yes	32
Previous radiotherapy	
No	59
Yes	40
Other metastases	
Visceral	
0	52
1	47
Skeletal (not spine)	
0	48
1	51

* As needed or daily dose.

decreases in the number of patients reporting pain were also observed at the last follow-up visit. Final follow-up analysis was available for 77 patients, 34 (44.2%) of whom reported pain at the last clinical visit (median follow-up time 6.1 months, range 1.0–56.6 months), a significant improvement over initial presentation ($p = 0.0002$) (Table 3).

Imaging Control

Follow-up MR images that could be analyzed for the presence of local recurrence were available for 39 patients with 52 lesions (median follow-up time 6.03 months, range

FIG. 1. Kaplan-Meier survival curve. Median survival time is 8.7 months.

1.1–42.9 months). Of these lesions, 11 (21.1%) exhibited local progression through increased canal narrowing or progressive growth.

Treatment Failure

For 4 patients, surgery was emergently performed after purported radiosurgery failure. For all 4, the indication for surgery was development of intractable back pain resulting from tumor progression and resultant mechanical instability. For 2 of these 4 patients, neurological deficits also developed before surgery.

By using the presence of pain at 3 months as an outcome, predictors of treatment failure were analyzed (Table 4). Univariate analysis indicated that the following were significant predictors of persistent pain after intervention: initial ESCC grade, stratified by a Bilsky grade of 1c ($p = 0.0058$); initial ASIA grade of D ($p = 0.011$); initial KPS score, stratified by a score of 80 ($p = 0.002$); the presence of multiple treated lesions ($p = 0.044$); and prior radiation at the site of interest ($p < 0.0001$). However, when multivariate analysis was performed on all variables with p values less than 0.05, the only predictor of pain at last follow-up visit was a prior history of radiation at the site of interest ($p = 0.0038$), although initial ESCC grade trended toward significance ($p = 0.073$).

Radiation Dosage

The radiation fractionation schemes used in this patient population are summarized in Table 5. The median

TABLE 3. Pain reported over time

Time After Treatment (mos)	No. of Patients			McNemar p Value
	Evaluated	Reporting Pain Initially	Reporting Pain During Follow-Up	
1	52	37	30	0.096
3	62	47	26	0.000072
6	46	33	14	0.00017
12	27	22	9	0.0019
Last follow-up	77	57	34	0.00020

FIG. 2. Trends in reported pain (A), narcotic usage (B), and steroid use (C).

dose prescribed was 21 Gy (range 6–54.9 Gy) delivered in a median of 3 fractions (range 1–33); median BED was 66.7 Gy. Whether the patient had received prior radiation at the level of interest was significantly associated with the final BED. Patients who had not received prior radiation

received a mean BED of 79.0 Gy (95% CI 73.7–84.3 Gy), and those who had received prior radiation received a mean BED of 60.6 Gy (95% CI 56.3–64.8 Gy) ($p < 0.0001$). The fitted values from the logistic regression analysis of pain at 3 months versus radiation dose showed that the

TABLE 4. Analysis of variables predictive of treatment success*

Variable	Treatment Failure at Last FU		Univariate Analysis			Multivariate Analysis
	No	Yes	OR	95% CI	p Value	p Value
Age			1.33	0.45–3.93	0.61	NI
<65	26	16				
≥65	11	9				
Initial ESCC score			9.56	2.09–54.17	0.0058	0.073
0–1b	17	4				
1c–3	4	9				
Initial ASIA grade			0.18	0.044–0.64	0.011	0.89
D	4	10				
E	33	15				
Initial KPS score			0.14	0.039–0.47	0.0020	0.32
<80	5	13				
≥80	32	12				
No. of treated lesions			3.6	1.07–13.44	0.044	0.39
1	32	16				
>1	5	9				
Decompressive surgery			2.87	0.98–8.76	0.057	NI
No	28	13				
Yes	9	12				
Previous radiotherapy			13.29	4.10–49.66	0.000041	0.0038
No	31	7				
Yes	6	18				
Visceral lesions			0.83	0.30–2.30	0.72	NI
No	19	14				
Yes	18	11				
Other skeletal lesions			1.59	0.57–4.48	0.38	NI
No	22	12				
Yes	15	13				

FU = follow-up; NI = not included.

* Boldface indicates statistical significance.

TABLE 5. Summary of radiation dosages

Prescription Dose (total radiation/fractions)	BED (Gy)	No. of Lesions
6/1	18	2
10/2	26.7	1
10/1	43.3	3
12/1	60	7
14/2	46.7	3
14/1	79.3	4
15/3	40	5
15/1	90	1
15/6	27.5	2
16/2	58.9	1
16/1	101.3	8
16/4	37.3	1
18/1	126	6
18/3	54	9
20/4	53.3	2
20/5	46.7	3
21/3	70	28
24/3	88	3
25/5	66.7	28
30/5	90	13
35/5	116.7	1
Total	Not applicable	131

median value of 66.7 Gy when used as a cutoff value had a predicted probability of pain at 3 months of 0.49. After radiation doses were dichotomized by this threshold, presence of pain at 3 months differed significantly between the 2 groups (OR 0.30, 95% CI 0.01–0.83) ($p = 0.02$), and a significant association was found between radiation dose and the presence of pain at 3 months ($p = 0.012$) (Fig. 3).

The association between radiographic canal impingement before treatment and BED trended toward significance among patients with Bilsky grades of 0–1b who received an average BED of 71.0 (95% CI 64.4–77.5 Gy) and patients with Bilsky grades of 1c–3 who received an average BED of 63.4 Gy (95% CI 59.0–67.9 Gy) ($p = 0.0874$).

The median maximum radiation dose to the spinal cord, thecal sac, or cauda equina was 16.4 Gy (range 0.6–42.8 Gy).

Complications

Among patients who did not undergo adjunctive surgical decompression, 6 (7.0% of lesions treated with SBRT only) *de novo* compression fractures occurred at treated levels for 5 patients. Of these 5 patients, 4 reported pain, which led to the discovery of the compression fractures, and the other patient, who had 2 simultaneously discovered compression fractures, was largely asymptomatic. Prior radiation to the affected level had been received by 2 of these 5 patients. These compression fractures were first documented at a median of 3.3 months (range 1–11.6 months) after initiation of SBRT. An additional patient experienced a compression fracture between fractions of her radiation treatment, prob-

ably because of preexisting structural weakness. Of the remaining lesions in the entire pool of patients, at least 37 (29.3%) demonstrated partial compression fracture or loss of vertebral height before treatment.

In total, 6 patients underwent vertebroplasty before SBRT, and another 4 patients underwent vertebroplasty for preexisting compression fractures after SBRT.

No radiation-induced myelopathy developed in any patient.

Discussion

Spinal metastases develop in 30%–90% of cancer patients at some point during their disease course.^{9,23,36,41} For some patients, these lesions are sometimes discovered during routine staging workups; but others experience pain or neurological deficits,²⁷ pain from compression of neural structures, or functional neurological compromise secondary to epidural extension.^{29,31} Although visceral metastases have a larger effect than spinal metastases on survival times,³⁷ the resulting decreases in quality of life have encouraged the development of new techniques to effectively manage spinal metastases.²⁴

Stereotactic radiosurgery is a well-accepted noninvasive method of managing spine lesions, and many studies have evaluated its efficacy.^{1,8,12–15,18,21,30,34,40,42} Previous studies have frequently included patients who survived more than 1 year after SBRT, and performance status distributions were generally favorable (Table 6). Additionally, in these studies, many patients underwent SBRT for disease recurrence after prior conventional radiation to the same level. As such, it is difficult to infer from these studies whether critically ill patients would still benefit from first-line radiosurgical intervention, particularly given their limited overall survival times. Our study included patients with a median survival time of 9.1 months and an actuarial 1-year survival rate of 43.7%. Additionally, patients often showed signs of advanced metastatic disease, and 53% had visceral metastases at the time of radiosurgery.

At last follow-up visit, 55.8% of patients were without local back pain attributable to vertebral body lesions. This finding is consistent with that of a study by Wang et al. that used a similar pain palliation metric as an outcome variable.⁴⁰ In that study, 6 months after SBRT, the proportion of patients reporting no pain increased from 26% initially to 54%,⁴⁰ a time that is comparable to our median final follow-up time of 6.1 months. Additionally, in our series, the proportion of patients reporting pain decreased significantly at 3, 6, and 12 months after radiosurgery. Although pain decreased significantly at these time points, the proportion of patients using narcotics and steroids did not decrease. These conflicting results may be the result of development of pain at other sites associated with increased disease or possibly the slow tapering of a steroidal medication dosage, the latter of which was not directly assessed in this study.

In our heterogeneous cohort, absence of local vertebral pain at 3 months after treatment was determined by whether radiation had previously been delivered to that level. Another predictor that trended toward significance was radiographic canal impingement ($p < 0.10$). With respect to

FIG. 3. Stratification of reported pain by BED. **Upper:** Box-and-whisker plot depicting the difference in BED between patients who reported pain at 3 months and those who did not. **Lower:** Scatter plot with logistic regression curve with confidence intervals showing the association between the radiation dose and the chances of having pain 3 months after treatment. Horizontal and vertical lines extending from a probability of 0.49 and a dose of 66.7 Gy are drawn to indicate the chosen threshold value. Figure is available in color online only.

canal impingement, rates of treatment success were higher for bone metastases that did not abut the spinal cord than for those that did contact the spinal cord. This finding is logical given the technical restrictions of SBRT and the need to meet strict cord tolerance doses during treatment planning. These data suggest that SBRT should be used with caution in patients with Bilsky Grade 1c or greater. This finding is consistent with that of a prior surgical series, which suggested that surgical decompression should be considered in patients with extensive epidural disease (i.e., Bilsky Grade 2 and higher) before treatment with SBRT.² This concept has been previously described as separation surgery, or surgical circumferential decompression.^{22,39} A recent study by Laufer et al. reported durable local control with use of separation surgery before SBRT; patients included in that study often experienced significant progression of epidural disease before treatment (Bilsky Grade 2 or 3 lesions for more than 70%), necessitating open surgical intervention.²²

Our findings, combined with results from previous reports, suggest that surgical intervention should be considered as the first-line strategy for patients with disease in

direct contact with the spinal cord, particularly in patients with instability or neurological deficits.²⁹ The optimal radiosurgical management of patients with significant epidural extension represents an area in need of future investigation. Optimization of radiation treatment regimens may lead to improved outcomes in this patient population, a conclusion that is in accordance with the results of the multivariate analysis. Specifically, threshold values for BEDs will be an important focus. Our data suggest that patients with lesions receiving a minimum BED of 66.7 Gy (the median BED of this study) had a greater than 50% chance of favorable pain outcomes 3 months after treatment.

The median prescribed dose in this series was 21 Gy delivered in 3 fractions, which is less aggressive than the doses reported for many other series.^{13,26,35} In part, this difference results from the fact that many (40.4%) of the patients included in our study had previously undergone radiation therapy at the same site. For those patients, prescription doses were reduced to meet normal tissue constraints. In addition, we included patients from our initial experience with spine SBRT, and doses became

TABLE 6. Summary of studies reported in the literature

Authors & Year	Median Survival (mos)	1-Yr Survival (%)	KPS Score		Mean Age or Range (yrs)
			80–100	50–70	
Ahmed et al., 2012	>12	52.2	NP		56.8
Garg et al., 2012	30.4	80*	48	13	60†
Patel et al., 2012	10.7	NP	NP		57–62
Wang et al., 2012	23	71.9	116	33	56.4
Sahgal et al., 2009	21	>50	39	0‡	57–59
Garg et al., 2011	22.5	76	45	14	60†
Gerstzen et al., 2007	>21§	>50	NP		56
Gagnon et al., 2009	10.5–14.5	NP	NP		56
Chang et al., 2007	24	>60	42	21	59†
Heron et al., 2012	13	>50	NP		59
Koyfman et al., 2012	12.8	>50	Median 80		58.5†
Yamada et al., 2008	15	>50	NP		62†
Present study	9.1	43.7	67	32¶	60.4

NP = not presented in the article.

* Approximate values determined from Kaplan-Meier curves.

† Mean ages were not available; reported values were median ages.

‡ KPS scores were all 70 or above in this cohort; no further information was provided.

§ Median follow-up time was 21 months; it can be assumed that median survival time was at least this long.

¶ For 1 patient, the reported KPS score was 40.

more aggressive as the experience of providers and confidence in the safety and reproducibility of the technique increased. At present, we aim to treat patients with the most hypofractionated dose schedule that allows for adequate tumor coverage while meeting normal tissue constraints. Several factors play into the decision, including tumor size and distance from critical structures such as the spinal cord and esophagus.

We report no cases of radiation-induced spinal cord myelopathy. We also report a 7.0% risk for de novo vertebral compression fractures, consistent with rates reported in prior studies (6.6%–11.0%).^{5,10,35} More aggressive dosing paradigms, such as single fraction doses above 20 Gy, have been associated with a higher risk for compression fractures.³⁵ However, higher BEDs may be associated with improved local control, and the current practice at our institution is to use more aggressive fractionation schedules than is reflected by the median reported in this series; many of these patients had received prior overlapping external beam radiation therapy.

Our study has several limitations. First, the primary outcome assessed in this study was local pain at the treated vertebral level, a parameter that is challenging to assess in a retrospective manner. To address this problem, data points corresponding to pain were collected only when clinical notes directly mentioned whether the patient had pain and thus pain was scored in a binary manner. Another key limitation was that many of our patients were lost to follow-up, preventing outcome assessment for all patients. This limitation applies especially to radiological outcomes, because most patients, unfortunately, did not undergo serial follow-up MRI. Last, to compare the wide variety of radiation dose prescriptions, we used the linear-quadratic BED estimation model. The accuracy of this model is questioned for doses per fraction outside the

range of 2–10 Gy.⁶ Nonetheless, in the absence of an alternative measure, the use of BED was our best method for comparing the wide variety of dose and fractionation schedules included in our analyses. However, the threshold BED (with an α/β of 3.0) dose derived in this study should be viewed with caution and merits further investigation.

This study investigates a heterogeneous study population characterized by many different tumor histologic types and radiation treatment schemes. Future studies with more controlled treatment regimens that focus on specific pathologies are needed.

Conclusions

Stereotactic radiosurgery is a well-accepted management option for spinal metastases in patients with advanced metastatic disease. Pain palliation occurs as early as 3 months, and significant differences in pain also occur at 6 and 12 months. The data presented in this article suggest more limited pain palliation for patients with tumors with epidural extension that deforms the cord or for patients who have previously received radiation to the same site. Further investigation into optimal doses and fractionation schedules is needed, but we report improved outcome in patients receiving a BED of 66.7 Gy or higher.

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