

Scientific Article

Oncologic and Functional Outcomes After Stereotactic Body Radiation Therapy for High-Grade Malignant Spinal Cord Compression



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Purpose: Although surgical decompression is the gold standard for metastatic epidural spinal cord compression (MESCC) from solid tumors, not all patients are candidates or undergo successful surgical Bilsky downgrading. We report oncologic and functional outcomes for patients treated with stereotactic body radiation therapy (SBRT) to high-grade MESCC.

Methods and Materials: Patients with Bilsky grade 2 to 3 MESCC from solid tumor metastases treated with SBRT at a single institution from 2009 to 2020 were retrospectively reviewed. Patients who received upfront surgery before SBRT were included only if postsurgical Bilsky grade remained ≥ 2 . Neurologic examinations, magnetic resonance imaging, pain assessments, and analgesic usage were assessed every 3 to 4 months post-SBRT. Cumulative incidence of local recurrence was calculated with death as a competing risk, and overall survival was estimated by Kaplan-Meier.

Results: One hundred forty-three patients were included. The cumulative incidence of local recurrence was 5.1%, 7.5%, and 14.1% at 6, 12, and 24 months, respectively. At first post-SBRT imaging, 16.2% of patients with initial Bilsky grade 2 improved to grade 1, and 53.8% of patients were stable. Five of 13 patients (38.4%) with initial Bilsky grade 3 improved to grade 1 to 2. Pain response at 3 and 6 months post-SBRT was complete in 45.4% and 55.7%, partial in 26.9% and 13.1%, stable in 24.1% and 27.9%, and worse in 3.7% and 3.3% of patients, respectively. At 3 and 6 months after SBRT, 17.8% and 25.0% of patients had improved ambulatory status and 79.7% and 72.4% had stable status.

Conclusions: We report the largest series to date of patients with high-grade MESCC treated with SBRT. The excellent local control and functional outcomes suggest SBRT is a reasonable approach in inoperable patients or cases unable to be successfully surgically downgraded.

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Introduction

Spinal metastases are common across malignancies and associated with substantial pain and functional limitations.¹ Approximately 10% of patients with spinal metastases will develop malignant epidural spinal cord compression (MESCC) during their disease course, leading to neurologic deficits and deterioration in a patient's quality of life.² Although the standard of care is upfront surgical decompression, as few as 15% of affected patients are eligible for this intervention.^{3,4} Optimal surgical candidacy relies on several patient and clinical factors, including but not limited to age, comorbidities, performance status, systemic burden of disease, number of vertebral levels involved, and preoperative motor function. Meanwhile, conventional radiation therapy (RT) alone is a noninvasive alternative, but given the restrictions on total dose that may be delivered in this manner, disease control is limited and reirradiation in the setting of recurrence may not be safe.^{3,5}

Conventional RT has typically had a palliative intent in the treatment of spinal metastases, focusing on alleviation of pain, prevention of fractures, and reversal or delay of neurologic deficits.⁶ More recently, stereotactic body radiation therapy (SBRT) has been increasingly employed to deliver a higher biologically equivalent dose, allowing both superior pain palliation compared with conventional RT⁷ as well as excellent local control (LC).⁸ However, the extent of epidural disease is a well-established predictor of LC,⁹⁻¹⁴ and MESCC is considered a relative contraindication of SBRT. Therefore, upfront surgical decompression before SBRT is highly recommended whenever possible to both allow for more immediate relief of spinal cord compression and reversal of neurologic deficits and to create space between the critical structures and gross disease. Nonetheless, alternative management options allowing more durable LC in inoperable cases (ie, in situations in which the spinal cord is unable to be successfully decompressed surgically) and in the reirradiation setting are crucial. Moreover, data evaluating SBRT alone in this setting are limited. The purpose of this study was to report the largest series to date of functional and oncologic outcomes for patients treated with SBRT for Bilsky grade 2 to 3 MESCC.

Methods and Materials

After institutional research board approval, patients treated with SBRT to vertebral metastases from solid tumors causing Bilsky grade 2 or greater spinal cord compression between 2009 and 2020 at a single tertiary academic radiation oncology center were retrospectively reviewed. Patients who were previously irradiated were included, and those who received upfront surgery before

SBRT were also eligible but included only if postsurgical Bilsky grade remained ≥ 2 , as confirmed typically by both magnetic resonance imaging (MRI) and/or myelogram. Target delineation was typically according to the consensus contouring guidelines for intact and postoperative spine metastases.¹⁵⁻¹⁸ The spinal cord planning risk volume was defined as the spinal cord on T2-weighted MRI (or computed tomography [CT] myelogram in cases of significant metal artifact) plus a 2-mm radial expansion. Below the conus, the thecal sac was generally used as the planning risk volume. Spinal cord constraints were set according to the 5% risk group in Sahgal et al,¹⁹ and all other normal tissue constraints followed American Association of Physics in Medicine Task Group-101.

Baseline patient and disease factors collected retrospectively included age, gender, performance status, primary disease site, prior irradiation status, and Bilsky grade. Pain level on the visual analog scale, motor strength examination, Frankel grade, ambulatory status, and 24-hour analgesic intake were also documented based on clinical notes. Motor strength was recorded as the lowest numerical motor strength documented on examination (0-5/5). Analgesic intake was converted to oral morphine-equivalent (OME) doses. Additionally, radiation treatment planning parameters of prescription dose/fractionation and isodose line were collected. Biologic effective dose (BED) was calculated using the equation $BED = D \times (1 + [d/(\alpha/\beta)])$, where D is the total dose in Gy, d is the dose per fraction, and the α/β was estimated to be 10 for all tumors.

For the cohort of patients who underwent surgery at the same vertebral level before receiving SBRT, the surgical technique was reviewed based on the operative report as well as review of the preoperative and postoperative imaging. Patients were grouped into laminectomy/indirect decompression alone, laminectomy/indirect decompression with concurrent fusion, separation surgery, and separation surgery with a full corpectomy and anterior reconstruction with a cage. For spinal stabilization, the method is to employ a standard pedicle screw/rod-based fixation with anywhere between 1 to 3 fixation points above and below the level of the index tumor site using titanium alloy screws and rods. The actual cord/cauda equina decompression and tumor resection is a "standard" separation surgery approach aiming at a complete thecal sac reconstitution on an intraoperative ultrasound.²⁰ The choice of whether to leave in a "spacer" or corpectomy defect biomechanical cage for anterior column reconstruction was left to the discretion of the surgeon based on extent of anterior column involvement by the tumor, perceived biomechanical instability presented weighed against the systemic disease status, and expected prognosis.¹¹ For patients who underwent either laminectomy alone or indirect decompression with fusion without formal separation surgery with pediculotomies and a ventral decompression, either the tumor was dorsally situated

and/or the indirect decompression was felt to be sufficient in providing thecal sac clearance at the time of surgery.

Based on institutional practice patterns, patients were generally followed with clinical evaluations and MRI at approximately 3-month time intervals after receiving SBRT. Pain response was defined as a combination of pain score and analgesic consumption, as recommended in international consensus guidelines.²¹ Pain relief compared with pre-SBRT reference was categorized as complete response (pain level was rated as a 0), partial response (either pain level decreased by ≥ 2 with the same or lower OME, or pain level was the same with $\geq 25\%$ decrease in OME), stable (same pain level and OME), or worse (higher pain level).⁷ Adverse events were recorded, and toxicity grades were determined according to National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. Radiographic local recurrence was defined as progressive disease on CT and/or MRI in the treatment volume or at the margin of the treatment field compared with imaging studies before SBRT. If unclear, the lesion was followed with a series of successive scans for further clarification, with the timing of local recurrence backdated to the date of the first indicative CT or MRI. Time to radiographic local recurrence was calculated with start date of SBRT as the reference time.

Competing risks analysis was used to estimate the cumulative incidence of local recurrence, using death from any cause as a competing event. Overall survival from SBRT start date was estimated using the Kaplan-Meier method. These analyses were repeated after stratifying groups by if they did or did not undergo surgery to the involved vertebral level within 90 days before SBRT. Baseline characteristics between the group who received surgery before SBRT and those who did not were calculated with χ^2 test and 2-tailed Student *t* test. *P* values were considered statistically significant when less than .05.

Results

One hundred and forty-three patients were included with a median follow-up of 8.0 months (range, 0.4-116.9 months). Table 1 includes a summary of patient demographics, disease characteristics, and treatment details. The median patient age was 56 years (range, 14-94 years), and 51.7% of patients were male. The most common histologies were non-small cell lung cancer (17.5%), breast cancer (16.8%), prostate cancer (11.2%), and sarcoma (11.2%). The majority (75.5%) of metastases were in the T-spine, whereas 22.3% were in the C-spine and 2.1% were in the L-spine. Only 30.8% of patients had a single involved vertebral level, whereas 24.5% had 2 consecutively involved levels, 31.5% had 3, and 13.3% had 4 or more. Bilsky grade 2 represented 90.9% of cases. About half (53.8%) of the patients underwent attempted

Table 1 Patient, lesion, and treatment characteristics

Patient characteristics (n = 143)	
Age in years, median (range)	56 (14-94)
Sex, n (%)	
Male	74 (51.7%)
Female	69 (48.3%)
Primary site, n (%)	
Lung	25 (17.5%)
Breast	24 (16.8%)
Prostate	16 (11.2%)
Sarcoma	16 (11.2%)
Kidney	15 (10.5%)
Colorectal	7 (4.9%)
Melanoma	6 (4.2%)
Head and neck	5 (3.5%)
Liver	4 (2.8%)
Pancreas	4 (2.8%)
Cholangiocarcinoma	3 (2.1%)
Esophageal	3 (2.1%)
Uterine	3 (2.1%)
Thyroid	3 (2.1%)
Other	9 (6.3%)
Baseline ECOG performance status, n (%)	
0	25 (17.5%)
1	71 (49.7)
2	28 (19.6%)
3	7 (4.9%)
Prior irradiation, n (%)	29 (20.3%)
Lesion and treatment characteristics	
Spinal location, n (%)	
Cervical	32 (22.3%)
Thoracic	108 (75.5%)
Lumbar	3 (2.1%)
Number of involved consecutive vertebral levels, n (%)	
1	44 (30.8%)
2	35 (24.5%)
3	45 (31.5%)
≥ 4	19 (13.3%)
Upfront surgery, n (%)	78 (54.5%)
Pre-SBRT Bilsky grade, n (%)	
2	130 (90.9%)
3	13 (9.1%)

(continued on next page)

Table 1 (Continued)

Patient characteristics (n = 143)	
Prescription dose, Gy, median (range)	25 (12-40)
Prescription isodose line, median (range)	60% (50%-85%)
Dose/fractionation (Gy x fx)	
12-14 Gy x 1	4 (2.8%)
8-9 Gy x 2	3 (2.1%)
6 Gy x 3	4 (2.8%)
7 Gy x 3	8 (5.6%)
8 Gy x 3	21 (14.7%)
9 Gy x 3	25 (17.5%)
4 Gy x 5	2 (1.4%)
5 Gy x 5	30 (21.0%)
6 Gy x 5	40 (28.0%)
BED10, Gy, mean (range)	44.4 (24.5-72.0)
Abbreviations: BED = biologic effective dose; ECOG = Eastern Cooperative Oncology Group; SBRT = stereotactic body radiation therapy.	

separation surgery before SBRT to persistent high-grade epidural disease. A majority of the patients (89.6%) underwent standard separation surgery or separation surgery with a full corpectomy and cage placement. More specifically, of the 77 patients who underwent prior surgery, 2 (2.6%) underwent laminectomy/indirect decompression alone, 6 (7.8%) underwent laminectomy/indirect decompression with fusion, 29 (37.7%) underwent separation surgery, and 40 (51.9%) underwent separation surgery + full corpectomy with anterior column reconstruction with cage. One-fifth (20.2%) of cases were in the reirradiation setting. Reirradiation occurred at a median time of 12 months (IQR, 7-19.5) after the previous course. The median prescription dose for the entire cohort was 25 Gy (range, 12-40 Gy) in a median of 5 fractions (range, 1-5). The radiation prescription doses were consistent between radiation naïve and reirradiation patients, and the most common dose regimens used were 6 Gy x 5

(28.0%), 5 Gy x 5 (21.0%), and 9 Gy x 3 (17.5%). The mean BED10 delivered was 44.4 Gy. The median prescription isodose line was 60% (range, 50%-85%).

At first post-SBRT imaging, 16.2% of patients with initial Bilsky grade 2 (n = 130) improved to grade 1 (6.2% to grade 1c, 9.2% to grade 1b, and 0.8% to grade 1a). The majority (53.8%) of patients remained grade 2. Four of 13 patients (30.8%) with initial Bilsky grade 3 remained stable, 4 (30.8%) improved to grade 2, and 1 patient (7.8%) improved to grade 1b. These results are shown in Fig. 1. Figure 2 displays the imaging and RT plan for a patient who demonstrated downgrading from Bilsky grade 3 to 1b after SBRT without preceding separation surgery.

The median overall survival was 10.7 months (range, 7.6-15.3). Overall survival was 65.1%, 47.2%, and 32.5% at 6, 12, and 24 months, respectively, as seen in Fig. 3a. The cumulative incidence of local recurrence was 5.1%, 7.5%, and 14.1% at 6, 12, and 24 months respectively, as seen in Fig. 3b. Figure 3c demonstrates overall survival and local recurrence outcomes after stratifying patients who underwent attempted separation surgery before SBRT with persistent high-grade MESCC and patients who did not have any surgery, and this showed no significant differences in overall survival (P = .248) and local recurrence (P = .100) between the groups. Of the 18 crude local recurrences occurring at a median of 9.7 months (range, 0.4-43.7), the most common histologies were renal cell carcinoma (4), non-small cell lung cancer (3), sarcoma (2), and uterine (2). One local recurrence was recorded after reirradiation. Only 9 patients underwent salvage surgery for recurrence at a median time of 11.1 months after SBRT (range, 2.0-16.7 months).

Table 2 includes a detailed summary of functional outcomes after SBRT. At 3 and 6 months after SBRT, there were 118 and 76 evaluable patients, respectively, for whom to report functional outcomes. At 3 months post-SBRT, 62.7% of evaluable patients ambulated with no assistance, compared with 48.3% of the same cohort pre-SBRT. At 3 and 6 months after SBRT, 17.8% and 25.0% of patients had improved ambulatory status and 79.7% and 72.4% had stable status. Before SBRT, the median pain score was 5 (IQR, 3-7) and median OME was 65 (IQR,

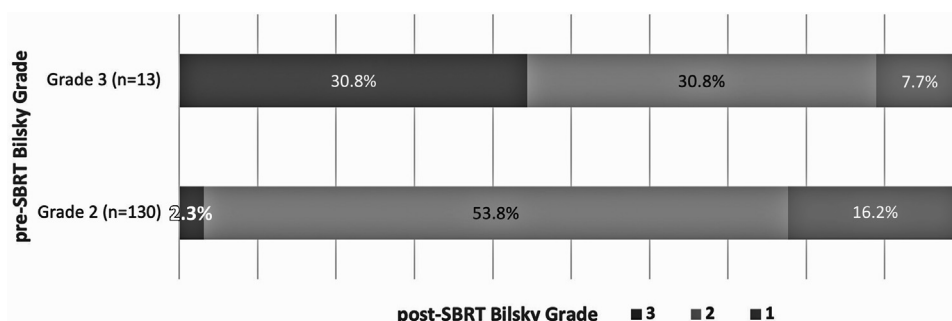


Figure 1 Bilsky epidural disease grades before and after stereotactic body radiation therapy.

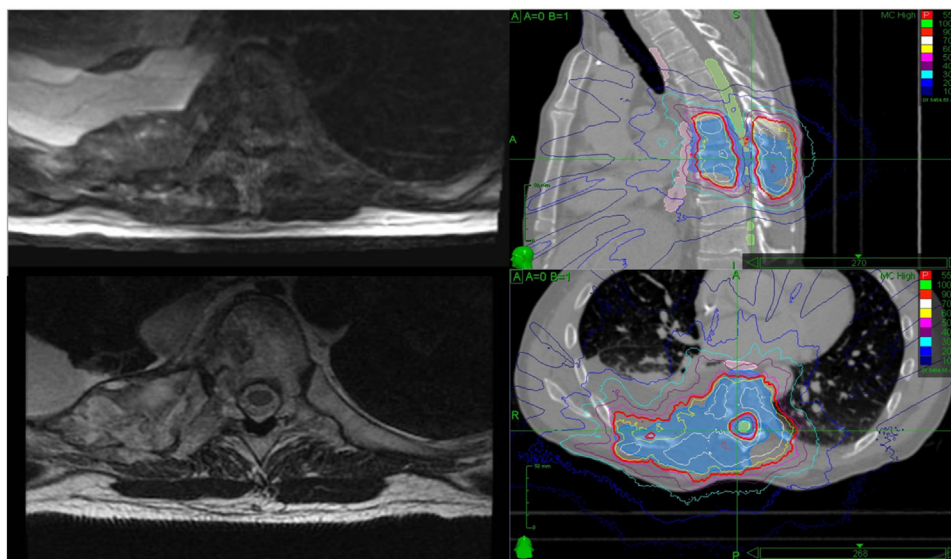


Figure 2 A patient with painful spine metastases from colon adenocarcinoma at T7-8 treated with SBRT 6 Gy x 5 fractions without prior separation surgery. Magnetic resonance imaging scans demonstrate Bilsky grade 3 before SBRT (a) and grade 1b at 3 months after SBRT (b). (c, d) The planning target volume in blue colorwash and isodose lines representing dose coverage of the target. This demonstrates sharp dose fall-off with respect to critical structures, such as the spinal cord + 2 mm expansion (green colorwash) and esophagus (pink colorwash).
Abbreviation: SBRT = stereotactic body radiation therapy.

12.5-144). Pain response is demonstrated in Fig. 4. At 3 and 6 months after SBRT, pain response was complete in 45.4% and 55.7%, partial in 26.9% and 13.1%, stable in 24.1% and 27.9%, and worse in 3.7% and 3.3% of patients, respectively. Patients who underwent attempted separation surgery were more likely to require assistance with ambulation ($P = .002$), have a worse Frankel grade ($P = .008$), a worse motor status ($P = .010$), and have another neurologic deficit ($P = .049$) before SBRT compared with those who had not undergone surgery before SBRT.

The crude post-SBRT vertebral compression fracture (VCF) rate was 18.1%. Seven of the 22 cases of VCF (31.8%) were associated with local progression. Of the remaining 15 VCF cases without recurrence, 7 required surgical intervention. The most common toxicities experienced were fatigue (44.8% of patients were grade 1; 27.3% grade 2), anorexia (23.1% grade 1; 6.3% grade 2), nausea (17.5% grade 1; 2.1% grade 2), and constipation (14.0% grade 1; 7.7% grade 2). Meanwhile, 4.2% of patients had recorded esophagitis and 3.5% had pain flare toxicities, but all cases were grade ≤ 2 . No patients developed spinal cord myelopathy.

Discussion

High-grade MESCC is associated with significant pain, weakness, and loss of independence with ambulation. Although surgical decompression and stabilization are the

standard of care for patients with high-grade MESCC, a subset of patients are not deemed surgical candidates or cannot afford a break in systemic therapy for surgical recovery. Although SBRT is being increasingly used in the management of intact and postoperative spine metastases with excellent LC,^{12,22-33} there are limited data supporting its use in patients with MESCC. We report oncologic and functional outcomes in the largest series to date of patients with high-grade MESCC treated with SBRT.

We report excellent oncologic outcomes with this approach, with 92.5% rate of LC at 1-year after SBRT. These results are comparable to previous series reporting 1-year LC of 70% to 95% for postoperative SBRT in patients with MESCC.^{8,34-36} Importantly, a significant proportion of our cohort (45.5%) did not receive surgery before SBRT. Existing data for SBRT without prior surgery to high-grade MESCC are limited to small cohorts, with 1 series reporting 1-year and 2-year LC rates of 89.6% and 78.0%,³⁷ similar to that of our cohort. Moreover, we observed promising rates of Bilsky grade stabilization or even downgrading of epidural disease in our cohort, who all had initial Bilsky grade 2 to 3 disease at the time of SBRT. This is important to prevent progressive neurologic deficits. Our results are consistent with prior prospective data in postoperative patients demonstrating a significant difference in Bilsky grade between postoperative imaging and 3 months post-SBRT imaging.²² Importantly, patients with high-grade epidural involvement demonstrate 1-year LC rates up to 95% if downgrading is observed compared with only 50% if

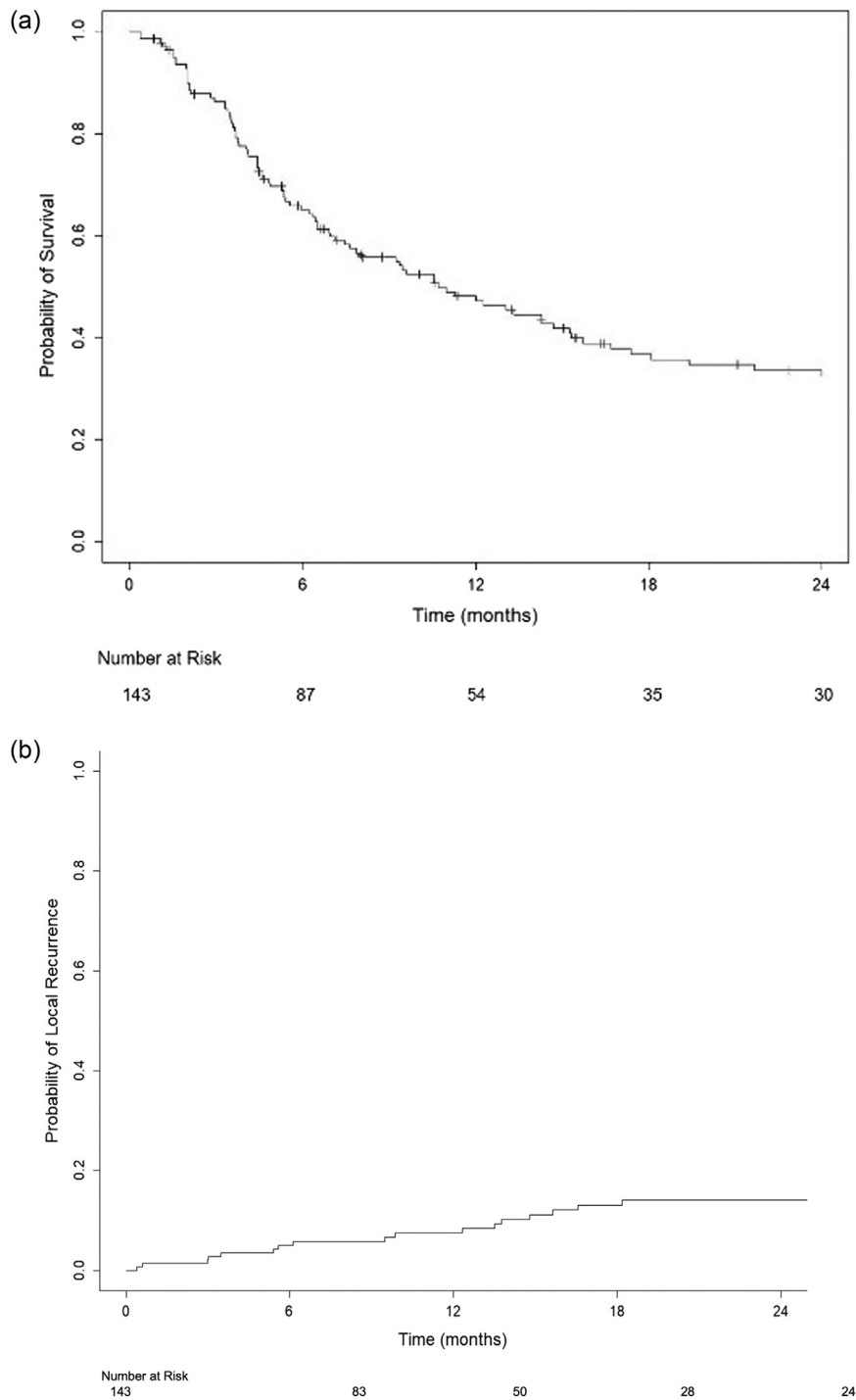


Figure 3 (a) Overall survival after stereotactic body radiation therapy for high-grade metastatic epidural spinal cord compression. (b) Cumulative incidence of local recurrence with death from any cause as a competing event after stereotactic body radiation therapy for high-grade metastatic epidural spinal cord compression. (c) Overall survival and local recurrence rates for those who underwent prior surgery and those who did not.

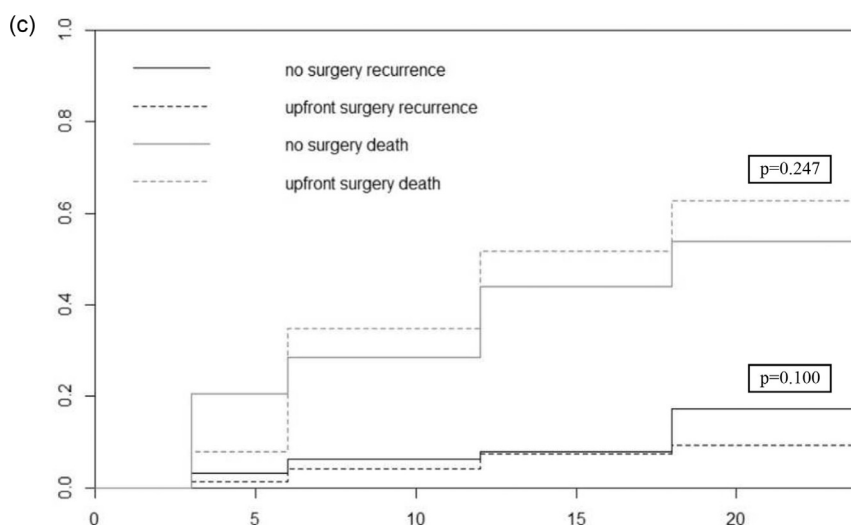


Figure 3 Continued.

downgrading is not achieved,^{12,38} and our data suggest that SBRT can be effective for both epidural disease downgrading and LC.

In line with our reported reasonable LC in patients receiving SBRT for MESCC, complete pain response can be maintained in this 3- and 6-month time frame, as demonstrated by 45% and 54.7% of patients in our cohort, respectively. Partial response was achieved in 26.9% of our cohort at 3 months and in 13.1% of patients at 6-months post-SBRT. This is consistent with a recently published randomized controlled phase 2/3 trial that reported superior rates of complete pain response at 3 months after SBRT compared with conventional RT (35% vs 14%).²¹ Furthermore, our data demonstrate that SBRT is effective at maintaining or improving ambulatory status for patients with high-grade MESCC, comparable to a smaller series, with 67% of patients with high-grade MESCC having a stable or improved ambulation status after SBRT.³⁹ This suggests that SBRT could serve as a favorable alternative should surgical decompression fail or not be an option.

Furthermore, our data suggest that reirradiation using SBRT is an acceptable option for previously irradiated patients with MESCC. Although separation surgery would allow superior dose delivery to the gross disease at the epidural margin, an invasive approach is not acceptable in all patients, particularly those with widely progressive disease and a poor prognosis. Ultimately, in terms of respecting cumulative lifetime dose limits to the spinal cord, SBRT serves an essential role in the reirradiation setting in its ability to deliver high BED to tumor with a steep dose gradient (ie, dose fall-off) adjacent to the cord,⁵ where reirradiation using conventional RT would often be rendered unsafe in that the plan would deliver the same dose to spinal cord as to the tumor. Importantly, one-fifth of our

cohort received prior radiation, but there were no cases of radiation-induced myelopathy.

It is important to note that of our 18 crude local recurrences, only 1 occurred in a patient with breast or prostate cancer, when these histologies represented 28% of our cohort and are also typically associated with longer survival/follow-up. Recurrences in our data set generally occurred in patients with radioresistant histologies (ie, sarcoma, renal cell carcinoma, and non-small cell lung cancer), such that dose escalation may help improve control. Although all patients should be encouraged to undergo surgical decompression when considered safe, surgery should be particularly emphasized for patients with radioresistant primaries given greater risk of local failure without dose escalation and the limited treatment options should these patients recur. In addition, the prescription doses in this series were conservative and more aggressive doses may be beneficial, especially in radioresistant tumors. Indeed, management of MESCC in the setting of recurrence or progression is challenging, particularly in medically inoperable patients or patients where pre-existing surgical hardware and irradiated tissue create a hostile surgical environment preventing optimal decompression.

Finally, although SBRT for MESCC should be used with caution, this study demonstrates safety of the approach. Specifically, there were no toxicities that were grade >2 and no patients developed spinal cord myelopathy. Our 18% rate of VCF is slightly higher than recent studies reporting rates around 10% to 15%, but it is likely that patients with MESCC have greater baseline instability, increasing risk of VCF compared with the general population receiving SBRT.^{38,40}

Several limitations exist in this study, including inherent selection bias from its retrospective nature. Information

Table 2 Functional outcomes after SBRT for high-grade MESCC

Functional outcomes	pre-SBRT (n = 143)			P value	3 mo post-SBRT (n = 118)			6 mo post-SBRT (n = 76)		
	All patients (n = 143)	Prior surgery (n = 78)	No prior surgery (n = 65)		All patients (n = 118)	Prior surgery (n = 67)	No prior surgery (n = 51)	All patients (n = 76)	Prior surgery (n = 42)	No prior surgery (n = 34)
Ambulation, n (%)				.002						
Independently	69 (48.3%)	28 (35.9%)	41 (63.0%)		74 (62.7%)	36 (53.7%)	38 (74.5%)	60 (78.9%)	30 (71.4%)	30 (88.2%)
With assistance	65 (45.4%)	42 (53.8%)	23 (35.4%)		40 (33.9%)	27 (40.3%)	13 (25.5%)	15 (19.7%)	11 (26.2%)	4 (11.8%)
None	9 (6.3%)	8 (10.3%)	1 (1.5%)		4 (3.4%)	4 (6.0%)	0 (0.0%)	1 (1.3%)	1 (2.4%)	0 (0.0%)
Worst motor strength, mean	4.0	3.98	4.49	.010	4.50	4.45	4.62	4.60	4.47	4.77
Other neurologic deficit, n (%)	45 (31.5%)	30 (38.5%)	15 (23.1%)	.049	15 (12.7%)	9 (13.4%)	6 (11.8%)	8 (10.5%)	6 (14.3%)	2 (5.9%)
Frankel grade, n (%)				.006						
E	69 (48.3%)	30 (38.5%)	39 (60.0%)		85 (72.0%)	44 (65.7%)	41 (80.4%)	59 (77.6%)	31 (73.8%)	28 (82.4%)
D	62 (43.4%)	38 (48.7%)	24 (36.9%)		29 (24.6%)	17 (25.4%)	12 (23.5%)	15 (19.7%)	11 (26.2%)	3 (8.8%)
C	10 (7.0%)	9 (11.5%)	1 (1.5%)		4 (3.4%)	3 (4.5%)	1 (2.0%)	2 (2.6%)	1 (2.4%)	0 (0.0%)

Abbreviations: MESCC = metastatic epidural spinal cord compression; SBRT = stereotactic body radiation therapy.

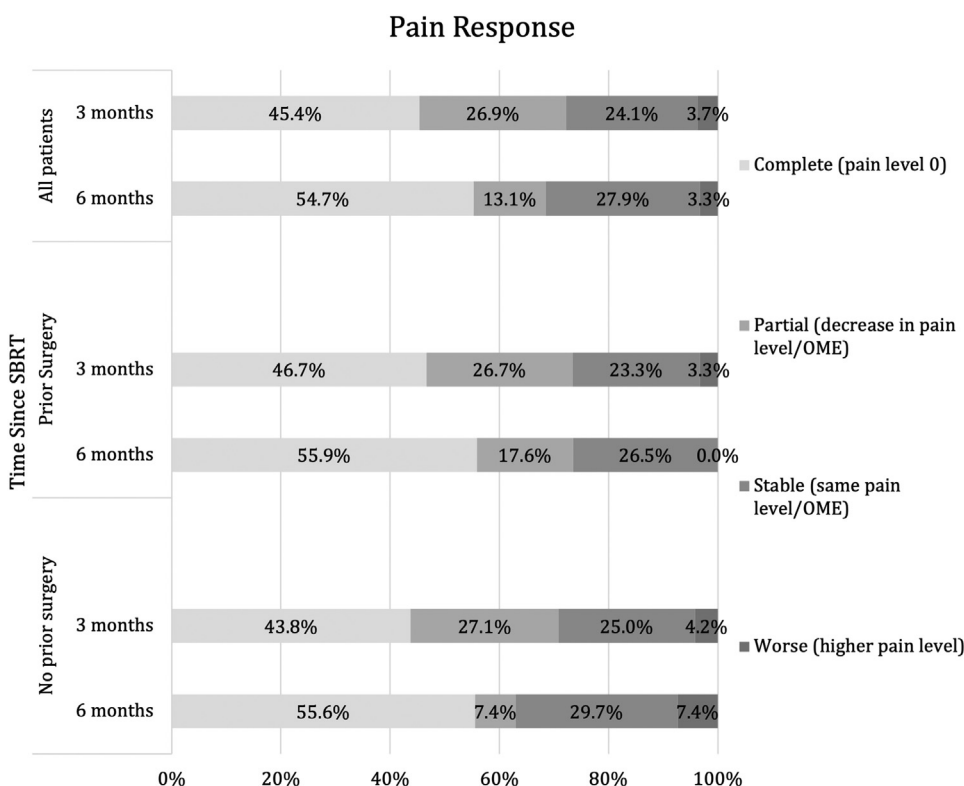


Figure 4 Pain response at 3 and 6 months after stereotactic body radiation therapy for all patients and stratified by those who underwent prior surgery and those who did not.

bias also exists, as pain score is a subjective measure and can vary based on several factors related to disease status. For instance, several patients had multiple spinal-level involvement or developed new metastases within the follow-up period, which likely modified the pain level reported. Motor strength assessed during a neurologic examination and amount of analgesics prescribed can also vary by the provider. Moreover, half (54.5%) of the patients in our cohort underwent surgery before SBRT, yet successful Bilsky downgrading (to grade <2) was not achieved. Unfortunately, we were unable to retrospectively capture the reasons why patients were either not surgical candidates or why epidural disease was not successfully surgically downgraded, limiting our understanding of the clinical scenarios where an SBRT-based approach would be most applicable. The baseline differences in the surgical and nonsurgical cohort limited our ability to compare outcomes for these 2 groups, but this was not the purpose of our study. Instead, we aimed to report oncologic and functional outcomes when SBRT is used to address persistent high-grade MESCC irrespective of surgical status. Given the poor overall prognosis of this patient population – as evidenced by our median survival of just under 11 months – long-term follow-up for SBRT outcomes is limited. Therefore, surgery should remain the standard of care until proven otherwise, and particular caution needs to be used in patients with anticipated long-term survival. However,

as life expectancy in the metastatic state increases, so too will the incidence of MESCC.³⁵ Understanding alternatives to surgical management will become increasingly essential for our aging cancer population, given that elderly patients are often deemed medically inoperable.^{41,42} Therefore, our findings provide important data for both LC and functional endpoints in SBRT for the management of high-grade MESCC.

Conclusion

To conclude, although level 1 data⁴ support upfront surgical decompression when possible, our excellent LC and safety profile suggest that SBRT is a reasonable approach for managing high-grade MESCC in patients who do not meet surgical criteria or who are unable to be successfully surgically downgraded.

Disclosures

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References

- Young RF, Post EM, King GA. Treatment of spinal epidural metastases. Randomized prospective comparison of laminectomy and radiotherapy. *J Neurosurg*. 1980;53:741-748.
- Mossa-Basha M, Gerszten PC, Myrehaug S, et al. Spinal metastasis: Diagnosis, management and follow-up. *Br J Radiol*. 2019;92:20190211.
- Donovan EK, Greenspoon J, Schnarr KL, et al. A pilot study of stereotactic boost for malignant epidural spinal cord compression: Clinical significance and initial dosimetric evaluation. *Radiat Oncol*. 2020;15:267.
- Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: A randomised trial. *Lancet*. 2005;366:643-648.
- Osborn VW, Lee A, Yamada Y. Stereotactic body radiation therapy for spinal malignancies. *Technol Cancer Res Treat*. 2018;17:1533033818802304.
- Steinberger JM, Yuk F, Doshi AH, Green S, Germano IM. Multidisciplinary management of metastatic spine disease: Initial symptom-directed management. *Neurooncol Pract*. 2020;7(Suppl 1):133-144.
- Sahgal A, Myrehaug SD, Siva S, et al. CCTG SC.24/TROG 17.06: A randomized phase II/III study comparing 24Gy in 2 stereotactic body radiotherapy (SBRT) fractions versus 20Gy in 5 conventional palliative radiotherapy (CRT) fractions for patients with painful spinal metastases. *Int J Radiat Oncol Biol Phys*. 2020;108:1397-1398.
- Blakaj DM, Palmer JD, Dibs K, et al. Postoperative stereotactic body radiotherapy for spinal metastasis and predictors of local control. *Neurosurgery*. 2021;88:1021-1027.
- Cao Y, Chen H, Sahgal A, et al. An international pooled analysis of SBRT outcomes to oligometastatic spine and non-spine bone metastases. *Radiother Oncol*. 2021;164:98-103.
- Kumar N, Madhu S, Bohra H, et al. Is there an optimal timing between radiotherapy and surgery to reduce wound complications in metastatic spine disease? A systematic review. *Eur Spine J*. 2020;29:3080-3115.
- Pennington Z, Pairojboriboon S, Chen X, et al. Utility of expanded anterior column resection versus decompression-alone for local control in the management of carcinomatous vertebral column metastases undergoing adjuvant stereotactic radiotherapy. *Spine J*. 2022;22:835-846.
- Al-Omar A, Masucci L, Masson-Cote L, et al. Surgical resection of epidural disease improves local control following postoperative spine stereotactic body radiotherapy. *Neuro Oncol*. 2013;15:1413-1419.
- Alghamdi M, Tseng CL, Myrehaug S, et al. Postoperative stereotactic body radiotherapy for spinal metastases. *Chin Clin Oncol*. 2017;6(Suppl 2):S18.
- Laufer I, Rubin DG, Lis E, et al. The NOMS Framework: Approach to the treatment of spinal metastatic tumors. *Oncologist*. 2013;18:744-751.
- Redmond KJ, Robertson S, Lo SS, et al. Consensus contouring guidelines for postoperative stereotactic body radiation therapy for metastatic solid tumor malignancies to the spine. *Int J Radiat Oncol Biol Phys*. 2017;97:64-74.
- Cox BW, Spratt DE, Lovelock M, et al. International Spine Radio-surgery Consortium consensus guidelines for target volume definition in spinal stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys*. 2012;83:e597-e605.
- Dunne EM, Sahgal A, Lo SS, et al. International consensus recommendations for target volume delineation specific to sacral metastases and spinal stereotactic body radiation therapy (SBRT). *Radiother Oncol*. 2020;145:21-29.
- Redmond KJ, Lo SS, Soltys SG, et al. Consensus guidelines for post-operative stereotactic body radiation therapy for spinal metastases: Results of an international survey. *J Neurosurg Spine*. 2017;26:299-306.
- Sahgal A, Chang JH, Ma L, et al. Spinal cord dose tolerance to stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2021;110:124-136.
- Barzilai O, Laufer I, Robin A, Xu R, Yamada Y, Bilsky MH. Hybrid therapy for metastatic epidural spinal cord compression: Technique for separation surgery and spine radiosurgery. *Oper Neurosurg (Hagerstown)*. 2019;16:310-318.
- Sahgal A, Myrehaug SD, Siva S, et al. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: An open-label, multicentre, randomised, controlled, phase 2/3 trial. *Lancet Oncol*. 2021;22:1023-1033.
- Redmond KJ, Sciubba D, Khan M, et al. A phase 2 study of post-operative stereotactic body radiation therapy (SBRT) for solid tumor spine metastases. *Int J Radiat Oncol Biol Phys*. 2020;106:261-268.
- Kowalchuk RO, Waters MR, Richardson KM, et al. Stereotactic radiosurgery for the treatment of bulky spine metastases. *J Neurooncol*. 2020;148:381-388.
- Chan MW, Thibault I, Atenafu EG, et al. Patterns of epidural progression following postoperative spine stereotactic body radiotherapy: Implications for clinical target volume delineation. *J Neurosurg Spine*. 2016;24:652-659.
- Harel R, Emch T, Chao S, et al. Quantitative evaluation of local control and wound healing following surgery and stereotactic spine radiosurgery for spine tumors. *World Neurosurg*. 2016;87:48-54.
- Sellin JN, Gressot LV, Suki D, et al. Prognostic factors influencing the outcome of 64 consecutive patients undergoing surgery for metastatic melanoma of the spine. *Neurosurgery*. 2015;77:386-393.
- Sellin JN, Suki D, Harsh V, et al. Factors affecting survival in 43 consecutive patients after surgery for spinal metastases from thyroid carcinoma. *J Neurosurg Spine*. 2015;23:419-428.
- Moulding HD, Elder JB, Lis E, et al. Local disease control after decompressive surgery and adjuvant high-dose single-fraction radiosurgery for spine metastases: Clinical article. *J Neurosurg Spine*. 2010;13:87-93.
- Bate BG, Khan NR, Kimball BY, Gabrick K, Weaver J. Stereotactic radiosurgery for spinal metastases with or without separation surgery. *J Neurosurg Spine*. 2015;22:409-415.
- Laufer I, Iorgulescu JB, Chapman T, et al. Local disease control for spinal metastases following "separation surgery" and adjuvant hypofractionated or high-dose single-fraction stereotactic radiosurgery: Outcome analysis in 186 patients. *J Neurosurg Spine*. 2013;18:207-214.
- Rock JP, Ryu S, Shukairy MS, et al. Postoperative radiosurgery for malignant spinal tumors. *Neurosurgery*. 2006;58:891-897.
- Gerszten PC, Germanwala A, Burton SA, Welch WC, Ozhasoglu C, Vogel WJ. Combination kyphoplasty and spinal radiosurgery: A new treatment paradigm for pathological fractures. *J Neurosurg Spine*. 2005;3:296-301.

33. Massicotte E, Foote M, Reddy R, Sahgal A. Minimal access spine surgery (MASS) for decompression and stabilization performed as an out-patient procedure for metastatic spinal tumours followed by spine stereotactic body radiotherapy (SBRT): First report of technique and preliminary outcomes. *Technol Cancer Res Treat*. 2012;11:15-25.
34. Ito K, Sugita S, Nakajima Y, et al. Phase 2 clinical trial of separation surgery followed by stereotactic body radiation therapy for metastatic epidural spinal cord compression. *Int J Radiat Oncol Biol Phys*. 2022;112:106-113.
35. Hu JX, Gong YN, Jiang XD, et al. Local tumor control for metastatic epidural spinal cord compression following separation surgery with adjuvant CyberKnife stereotactic radiotherapy or image-guided intensity-modulated radiotherapy. *World Neurosurg*. 2020;141:e76-e85.
36. Faruqi S, Chen H, Fariselli L, et al. Stereotactic radiosurgery for postoperative spine malignancy: A systematic review and international stereotactic radiosurgery society practice guidelines. *Pract Radiat Oncol*. 2022;12:e65-e78.
37. Rothrock RJ, Li Y, Lis E, et al. Hypofractionated spinal stereotactic body radiation therapy for high-grade epidural disease. *J Neurosurg Spine*. 2020;33:680-687.
38. Chen X, Gui C, Grimm J, et al. Normal tissue complication probability of vertebral compression fracture after stereotactic body radiotherapy for de novo spine metastasis. *Radiother Oncol*. 2020;150:142-149.
39. Lee I, Omodon M, Rock J, Shultz L, Ryu S. Stereotactic radiosurgery for high-grade metastatic epidural cord compression. *J Radiosurg SBRT*. 2014;3:51.
40. Faruqi S, Tseng CL, Whyne C, et al. Vertebral compression fracture after spine stereotactic body radiation therapy: A review of the pathophysiology and risk factors. *Neurosurgery*. 2018;83:314-322.
41. Desai R, Nayar G, Suresh V, et al. Independent predictors of mortality following spine surgery. *J Clin Neurosci*. 2016;29:100-105.
42. Weir HK, Thompson TD, Stewart SL, White MC. Cancer incidence projections in the United States between 2015 and 2050. *Prev Chronic Dis*. 2021;18:1-8.