Spinal stereotactic body radiotherapy following intralesional curettage with separation surgery for initial or salvage chordoma treatment

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OBJECTIVE Chordoma is a rare malignant tumor for which en bloc resection with wide margins is advocated as primary treatment. Unfortunately, due to anatomical constraints, en bloc resection to achieve wide or marginal margins is not feasible for many patients as the resulting morbidity would be prohibitive. The objective of this study was to evaluate the efficacy of intralesional curettage and separation surgery followed by spinal stereotactic body radiation therapy (SBRT) in patients with chordomas in the mobile spine.

METHODS The authors performed a retrospective chart review of all patients with chordoma in the mobile spine treated from 2004 to 2016. Patients were identified from a prospectively collected database. Initially 22 patients were identified with mobile spine chordomas. With inclusion criteria of cytoreductive separation surgery followed closely by SBRT and a minimum of 6 months of follow-up imaging, 12 patients were included. Clinical and pathological characteristics of each patient were collected and data were analyzed. Patients were divided into two cohorts—those undergoing intralesional resection followed by SBRT as initial chordoma treatment at Memorial Sloan Kettering Cancer Center (MSKCC) (Cohort 1) and those undergoing salvage treatment following recurrence (Cohort 2). Treatment toxicities were classified according to the Common Terminology Criteria for Adverse Events version 4.03. Overall survival was analyzed using Kaplan-Meier analysis.

RESULTS The 12 patients had a median post-SBRT follow-up time of 26 months. Cohort 1 had 5 patients with median post-SBRT follow-up time of 65.9 months and local control rate of 80% at last follow-up. Only one patient had disease progression, at 48.2 months following surgery and SBRT. Cohort 2 had 7 patients who had been treated at other institutions prior to undergoing both surgery and SBRT (salvage therapy) at MSKCC. The local control rate was 57.1% and the median follow-up duration was 10.7 months. One patient required repeat irradiation. Major surgery- and radiation-related complications occurred in 18% and 27% of patients, respectively. Epidural spinal cord compression scores were collected for each patient pre- and postoperatively.

CONCLUSIONS The combination of surgery and SBRT provides excellent local control following intralesional curettage and separation surgery for chordomas in the mobile spine. Patients who underwent intralesional curettage and spinal SBRT as initial treatment had better disease control than those undergoing salvage therapy. High-dose radiotherapy may offer several biological benefits for tumor control.

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KEY WORDS chordoma; separation surgery; radiosurgery

CHORDOMA is a rare, primary spinal malignant neoplasm that arises from the remnants of the embryonic notochord.^{23,50,57} Chordoma has a reported incidence of less than 0.1 per 100,000 people per year but is the most frequent of the primary spinal tumors⁶ and often

presents with vague, indolent symptoms.^{6,23,30} Given their relatively slow malignant growth, chordomas are often diagnosed late in the disease process and involve critical structures, creating challenging treatment needs for these complex cases. Physicians commonly use the Enneking

ABBREVIATIONS CTCAE = Common Terminology Criteria for Adverse Events; ESCC = epidural spinal cord compression; MSKCC = Memorial Sloan Kettering Cancer Center; SBRT = stereotactic body radiation therapy.

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staging system, designed to describe primary musculoskeletal tumors, when discussing treatment and prognosis for spine tumors including chordoma.¹⁸ En bloc resection with wide margins to prevent seeding and recurrence has been advocated as the only means to achieve cure,⁶ whereas intralesional resection without effective adjuvant therapy has proven to be less effective for local control.^{32,59,62} En bloc resection is invasive and often associated with a high risk for complication, but it has proven to be effective in lengthening survival and maintaining local control better than any other method shown to date.^{3,4,6,7,9,13,17,20,25,27,34,39,42–44,49,55}

While en bloc resection is the treatment of choice for chordoma, not all chordomas are conducive to en bloc resection to achieve marginal or wide margins due to their relationship to other vital structures such as the spinal cord or vertebral arteries.^{23,31} However, some authors have argued that aggressive resection is indicated even in the face of severe neurological sacrifice. With up to 32% of reported chordomas arising in the mobile spine, there remains a need to explore alternatives to traditional en bloc treatment in such complex cases with unique anatomical constraints.^{31,38} While traditionally thought to be the quintessential radioresistant tumor, chordomas have recently been shown to respond positively to surgery followed by adjuvant single-fraction stereotactic body radiation therapy (SBRT).³¹ With improved technology and the ability to define more conformal radiation margins, single-fraction SBRT provides a safer alternative for tumors not amenable to en bloc resection with wide margins while still achieving appropriate tumor control and preventing disease progression.³¹ We report on a single-institution series of 12 patients who underwent intralesional resection with separation surgery followed by adjuvant SBRT.

Methods

IRB approval was obtained. We identified 22 patients with a histologically confirmed diagnosis of chordoma in the mobile spine who underwent resection followed by SBRT at Memorial Sloan Kettering Cancer Center (MSKCC) from 2004 to 2016. Patients who underwent spinal SBRT within 4 months following surgery were included. Patients were considered to have undergone SBRT if they had received 5 or fewer fractions of high-dose radiation. Of the 22 patients undergoing resection, 13 met inclusion criteria of having undergone resection followed by SBRT treatment as defined above. One patient was excluded because of a lack of follow-up imaging. The remaining 12 patients were subsequently divided into two cohorts: Cohort 1 was composed of those whose initial chordoma treatment was at MSKCC and Cohort 2 was composed of those whose initial treatment was elsewhere and whose current salvage treatment was at MSKCC. Cohort 1 contained 5 patients and Cohort 2 contained 7 patients.

Patient and tumor characteristics, treatments, and follow-up information were collected through a retrospective review of a prospectively maintained database. Each patient had at least one documented imaging modality for review. For each patient, all imaging and radiology reports (CT, MRI, and plain radiography) were reviewed from

the time of treatment until last follow-up for evidence of progression. Dates of all posttreatment images showing progression were noted and used for analysis of progression-free survival. Progression-free survival was defined as the time between SBRT and the next imaging modality demonstrating evidence of disease progression. Pretreatment, posttreatment, and follow-up MRI images were further reviewed to determine epidural spinal cord compression (ESCC) scores⁵ at the time of treatment, immediately posttreatment, and at the time of last follow-up. Treatment complications were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4. IBM SPSS statistical software was used to perform Kaplan-Meier analysis.

Spine SBRT was performed as previously described.⁶¹ Briefly, patients underwent simulation with CT images with 2-mm slice thickness. A myelogram or MRI fusion was used to delineate spinal cord anatomy and tumor volumes. Patients were immobilized using a patient-customized cradle for both simulation and treatment.⁶⁰ Treatment planning was performed using either Top Module (MSKCC, in-house software) or Eclipse (Varian Medical Systems); we used an inverse treatment planning—typically 5–7 radiation beams around a single isocenter with intensity modulation controlled with multileaf collimators. The gross tumor volume was outlined according to CT and MRI images after consensus review by the treating radiation oncologist and neurosurgeon. The clinical target volume encompassed gross tumor volume and areas of potential microscopic spread. The planning target volume was a 2-mm expansion from the clinical target volume, excluding the thecal sac and also the esophagus if abutting gross tumor volume. The prescribed dose ranged from 24 Gy in 1 fraction to 24–36 Gy in 3 fractions, and the dose was prescribed to the 100% isodose line as allowed by dose constraints for organs-at-risk such as the spinal cord, esophagus, and bowels. Treatment was delivered with a LINAC (linear accelerator) using 6-mV and/or 15-mV photons. Cone-beam CT scans were used to verify patient positioning prior to treatment.

Results

Twelve patients met the inclusion criteria. Patient and tumor characteristics are summarized in Table 1. The majority of patients were men (75%), and the median age at surgery was 59 years (range 47–81 years). The median time between surgery and SBRT was 40 days (range 19–124 days). The median follow-up duration from SBRT was 26 months (range 1.7–89 months). Six cervical, 4 thoracic, and 2 lumbar spine tumors were treated.

Radiation treatment details are shown in Table 2. The majority of patients were treated with either 24 Gy in 1 fraction or 27 Gy in 3 fractions, while the remaining patients were treated in 3 fractions to a total dose ranging from 24 Gy to 36 Gy. Four patients (33%) received p32 plaque brachytherapy intraoperatively at the time of surgical curettage. Six patients overall (50%), all in Cohort 2 (85.7%), had received prior radiation at the site—4 received prior SBRT and 2 received prior radiation therapy with conventional fractionation.

TABLE 1. Patient and tumor characteristics

Patient Characteristics	All Patients (n = 12)	Cohort 1 (n = 5)	Cohort 2 (n = 7)
Age at op, median (range), yrs	59 (47–81)	61 (56–81)	59 (47–78)
Age group, no. (%), yrs			
≤55	1 (8)	0 (0)	2 (28.6)
55–64	6 (46)	3 (60)	2 (28.6)
≥65	6 (46)	2 (40)	3 (42.8)
Sex, no. (%)			
Male	8 (62)	2 (40)	5 (71.4)
Female	5 (38)	3 (60)	2 (28.6)
Days btwn op & SBRT, median (range)	40 (19–124)	40 (22–50)	40 (19–124)
Mos btwn SBRT & last FU, median (range)	37.3 (1.7–89)	65.4 (14–89)	10.7 (1.7–82)
Levels treated, no. (%)			
Cervical	6 (50)	3 (60)	3 (42.8)
Thoracic	4 (33.3)	1 (20)	3 (42.8)
Lumbar	2 (16.7)	1 (20)	1 (14.3)

FU = follow-up.

Surgical and SBRT complications are detailed in Table 3. Overall, 75% of patients experienced complications, with 41.7% experiencing CTCAE Grade 3 or higher complications. There were 2 Grade 1 toxicities, 4 Grade 2 toxicities, 4 Grade 3 toxicities, and 1 Grade 4 toxicity reported. There were no reported Grade 5 toxicities.

TABLE 2. Radiation treatment characteristics

Radiation Characteristics	No. of Patients (%)		
	All Patients (n = 12)	Cohort 1 (n = 5)	Cohort 2 (n = 7)
SBRT dose & fractionation			
24 Gy/1 fraction	6 (50)	3 (60)	3 (42.8)
24 Gy/3 fractions	1 (8.3)	0 (0)	1 (14.3)
27 Gy/3 fractions	3 (25)	2 (40)	1 (14.3)
30 Gy/3 fractions	1 (8.3)	0 (0)	1 (14.3)
36 Gy/3 fractions	1 (8.3)	0 (0)	1 (14.3)
Intraop p32 plaque brachytherapy			
No	8 (67)	4 (80)	4 (57.1)
Yes	4 (33)	1 (20)	3 (42.8)
Prior radiation at site			
No	6 (50)	5 (100)	1 (14.3)
Yes	6 (50)	0 (0)	6 (85.7)
No. of contiguous levels treated w/ SBRT			
1	3 (25)	2 (40)	1 (14.3)
2	1 (8.3)	1 (20)	0 (0)
3	5 (41.7)	1 (20)	4 (57.1)
4	3 (25)	1 (20)	2 (28.6)

TABLE 3. Surgical and radiation complications

CTCAE	All Patients	Cohort 1		Cohort 2	
		No.	Toxicity	No.	Toxicity
Grade 1	2	1	Compression fracture	1	Dermatitis
Grade 2	4	4	Dysphagia, xerostomia, MRI spinal cord signal change, DVT	0	NA
Grade 3	4	4	Dysphagia, mucositis, hardware failure, vocal cord paralysis	0	NA
Grade 4	1	0	NA	1	Wound dehiscence

DVT = deep vein thrombosis; NA = not applicable.

Grade 1 toxicities included dermatitis and fracture. Grade 2 toxicities included dysphagia, xerostomia, spinal cord T2 signal change on MRI, and deep vein thrombosis. Radiation-associated major complications occurred in 27% of patients, and included dysphagia, mucositis, and vocal cord paralysis that occurred 4 years after radiation therapy. Two complications directly related to surgery included a rod fracture that occurred 4 years postoperatively and a wound dehiscence after a reoperation for tumor recurrence in Cohort 2, resulting in a surgical complication frequency of 18%.

Table 4 provides a summary of clinical information for each patient. Of the 5 patients in Cohort 1, only 1 had local progression at last follow-up, resulting in a local control rate of 80% at last follow-up. Cohort 1 had a median post-SBRT follow-up period of 65.9 months; Cohort 2 had a median follow-up duration of 10.7 months, with 3 patients having progression, for a local control rate of 57.1% at last follow-up.

Kaplan-Meier curves for overall survival are shown in Fig. 1. At 2 years, actuarial overall survival was 80% for Cohort 1 and 85.7% for Cohort 2. The mean actuarial estimations of overall survival were 76.6 months (95% CI 50.1–103.2 months) and 68.6 months (95% CI 32–104.6 months) for Cohort 1 and for Cohort 2, respectively. Analysis of combined cohort data revealed an estimated overall survival of 77.6 months (95% CI 52–103.3 months).

Illustrative Cases

Cohort 1

A 57-year-old woman presented with a 6-month history of neck stiffness and hand clumsiness. She also reported a 1-month history of anterior thigh hyperesthesia but denied weakness, numbness, or vesicorectal dysfunction. MRI of the cervical spine, ordered by her primary care physician, revealed a mass involving the C-5 and C-6 vertebral bodies (Fig. 2A) with a large epidural component and severe spinal cord compression (ESCC Grade 3) with spinal cord edema. Examination revealed full strength throughout but diminished dexterity in both hands. She underwent CT-guided needle biopsy, the results of which revealed a chordoma. She was started on a course of dexamethasone and scheduled for surgery. She underwent C4–7 lami-

TABLE 4. Radiation and surgical characteristics by patient

Patient No.	Sex	Age	Tumor Location	No. of Previous Ops	Previous RT Gy/ No. of Fractions	SBRT Dose Gy/ No. of Fractions	ESCC Score			Time to Progression (mos)	Overall Survival (mos)	Complications (CTCAE Grade)	Cause of Death
Cohort 1													
1	M	81	T12	NA	NA	27/3	3	1c	NA	NA	52.3	NA	NA
2	F	57	C4–C6	NA	NA	24/1	3	1b	0	NA	67.9	Vocal cord paralysis (3)	NA
3	F	61	C1–C3	NA	NA	24/1	3	1a	0	48.2	91.9	Dysphagia (3)	NA
4	F	56	C2	NA	NA	24/1	1c	1b	1a	NA	16.0	Dysphagia (2), xerostomia (2), mucositis (3), T2 cord signal change (2)	GI hemorrhage
5	M	75	L4	NA	NA	24/1	1c	0	0	NA	72.2	L-4 compression fracture (1), rod fracture (3),* DVT (2)*	NA
Mean									48.2	60.1			
Median									48.2	67.9			
Cohort 2													
6	M	77	L2	1	27/3	24/1	3	1b	NA	76.3	105.9	Wound dehiscence requiring plastic surgery (4)*	Sepsis
7	M	56	C4–C6	2	74/40	24/3	3	1c	NA	1.9	63.2	RUE paresis (2)	Unknown
8	M	55	T5–T7	1	36/3	24/1	3	1a	1a	NA	59.9	Dermatitis (1), RT myelitis (1)	NA
9	M	59	T3–T4	1	30/3	30/3	3	0	NA	NA	1.7	RUE paresis (2)	Meningitis
10	F	67	T11–L1	5	17.7/5	27/3	3	3	NA	2.9	69.5	None	NA
11	M	78	C4–C5	2	NA	36/3	3	2	1b	NA	27.1	RUE paresis (2)	NA
12	M	47	T9–T11	1	70/39	24/1	1b	1a	0	NA	32.0	None	Unknown
Mean										27.0	51.3		
Median										2.9	59.9		
Overall													
Mean										32.3	55.0		
Median										25.6	61.6		

GI = gastrointestinal; RT = radiation therapy; RUE = right upper extremity.

* Indicates surgical complication.

nectomies, resection of the epidural component of the tumor, posterior C2–T2 instrumented fusion, C-5 and C-6 corpectomies, placement of a Harms titanium mesh cage (DePuy Spine), and anterior plate fixation (Fig. 3). A p32 plaque was also placed intraoperatively to deliver temporary high-dose irradiation. Her immediate postoperative ESCC grade was 1b (Fig. 2B). She had, as anticipated, self-limited mild dysphagia in the perioperative period, and her hand coordination improved. She underwent adjuvant single-fraction radiation treatment, to 24 Gy, 2 months postoperatively. Most recent imaging, 5.25 years later, showed continued tumor control, with ESCC score of 0 (Fig. 2C). She developed delayed radiation-associated unilateral vocal cord paralysis several years postoperatively, for which she underwent a vocal cord medialization and for which symptomatic recovery was good. She remains ambulatory and had a Karnofsky Performance Scale score of 90 at last follow-up.

Cohort 2

A 78-year-old man with a history of melanoma initially presented to an outside institution with progressive right hand pain. MRI of the spine revealed a C-5 centered mass with cranial and caudal epidural extension as well as high-grade spinal cord compression. He underwent C-5 corpectomy with intralesional curettage and C3–7 laminectomies and placement of posterior instrumentation at the outside institution. Intraoperative pathological examination revealed chordoma. He was recommended radiotherapy at that time but refused, electing for observation. Five months later, MRI showed progression of his residual tumor. Subsequent MRI, then 8 months after surgery, demonstrated significant progression of disease (ESCC Grade 3), with encasement and displacement of the right vertebral artery, and encasement of the C-5 and C-6 nerve roots on the right. He underwent repeat resection and decompression of the spinal cord at the same outside institution.

FIG. 1. Kaplan-Meier curve for overall survival for Cohort 1 (blue) and Cohort 2 (green) after surgery followed by SBRT.

He subsequently sought care at MSKCC when his right hand pain returned and he developed proximal Grade 3/5 right upper-extremity weakness. MRI demonstrated aggressive recurrence with ESCC Grade 3 (Fig. 4A). He then underwent repeat anterior and posterior cervical resection with removal of epidural tumor and intraoperative radiation with a p32 plaque. Postoperatively his ESCC score was 2 (Fig. 4B). One month postoperatively he received SBRT (total dose 36 Gy given in 3 fractions). His most recent imaging study (9 months) revealed excellent tumor control with ESCC score of 1b (Fig. 4C). His proximal

FIG. 2. Imaging for Patient 2 in Cohort 1. **A:** Preoperative axial and sagittal MR images demonstrating ESCC Grade 3. **B:** Postoperative axial MR image demonstrating ESCC Grade 1b. **C:** Long-term follow-up axial MR image demonstrating progressive resolution of chordoma, now ESCC Grade 0.

FIG. 3. Anteroposterior (A) and lateral (B) postoperative radiographs demonstrating anterior and posterior instrumented fixation.

right upper-extremity weakness did not improve and he has home health assistance.

Discussion

While data accumulate on proton⁵⁸ and carbon ion radiotherapy^{29,52} for treatment of chordoma, there is growing evidence for high-dose-per-fraction conformal photon irradiation as well. Single-fraction high-dose spinal radiosurgery has been shown to achieve local control in greater than 90% of metastatic tumors, even to traditionally classified radioresistant tumors such as melanoma and renal cell carcinoma.⁶⁰ Additionally, several small studies have demonstrated promising results using radiosurgery for skull base chordomas,^{35–37} as well as mobile spine and sacral chordomas.⁶¹ Photon therapy has advantages compared with particle radiation in that it is more accessible, and spinal hardware does not diminish photon therapy efficacy while hardware does affect the efficacy of par-

FIG. 4. Imaging for Patient 11 in Cohort 2. **A:** Preoperative axial and sagittal MR images demonstrating ESCC Grade 3. **B:** Postoperative axial MR image demonstrating ESCC Grade 2. **C:** Axial MR image 8 months post-SBRT demonstrating continued retraction of the tumor and ESCC 1b.

ticle therapy.⁴⁶ In this series we present effective control of chordoma without the use of en bloc resection with wide margins, but with curettage, intralesional resection or separation surgery followed by high-dose conformal radiation therapy. As seen in the two case examples, tumor volume decreases following intralesional surgery and high-dose SBRT as evidenced by the change in ESCC score. Patients are spared morbidity but achieve adequate tumor control. While chordomas have been considered radioresistant, the response to high-dose SBRT is encouraging. High-dose-per-fraction radiation may offer radiobiological advantages compared with conventionally fractionated radiotherapy when treating chordomas.⁶¹ Higher doses may result in greater irreparable and lethal DNA damage¹⁰ and may also have the additional advantage of inducing tumor endothelial dysfunction, a phenomenon observed in high-dose treatments.²² Additionally, high-dose-per-fraction radiation may stimulate a cytotoxic T-cell-mediated immunogenic effect, further potentiating radiotherapy.³³

Molina et al. presented a multiinstitutional case series in which en bloc resection of cervical chordomas was attempted.⁴⁰ Upper cervical spine (C-1 and C-2) chordomas were associated with a dramatically higher rate of complications compared with subaxial chordomas (71% vs 22%, respectively) and higher rates of recurrence. Given the complex vascular, osseoligamentous, and important neuroanatomy that presents unique surgical challenges in cases of atlantoaxial chordomas, and given the significantly higher rate of complications, the authors advocated intralesional resection for C-1 and C-2 chordomas rather than en bloc resection. Our study provides further support to their conclusion, as the one recurrence in Cohort 1 occurred in the case of a C1–3 chordoma. This patient has obtained durable control after intralesional curettage and high-dose-per-fraction photon irradiation in a follow-up period of nearly 92 months. Following 48.2 months of progression-free survival after initial surgery and SBRT, the patient then underwent a second radiation treatment in which 27 Gy of radiation was delivered in 3 fractions without further surgery, providing an additional 43.6 additional months of local control while sparing the patient the increased risk of neurological morbidity from attempted en bloc resection.

In this series, patients in Cohort 1 experienced better outcomes with a local tumor control rate of 80%, while patients in Cohort 2 had a local tumor control rate of 57.1%. Furthermore, among patients who had disease progression, the median time to progression was 48.2 months compared to a median of 2.9 months in Cohort 2 (Table 4). Since local control was greater than 50% in both cohorts, a median time to failure was not reached. Of those in Cohort 2 whose treatment failed, 2 of the 3 patients had rapid disease progression following treatment. Patients with chordoma often undergo multiple operations, and the first operation is the best chance at optimal outcome.⁶ Our data are consistent with this “first shot” principle and with Choi et al., who found that patients who had undergone prior resections at outside institutions before seeking treatment at specialized centers had lower survival rates.¹²

Although the possibility of “seeding” was previously described as strong evidence for en bloc resection,² it is noteworthy that no patients in this study demonstrated re-

currence along the surgical tract of the surgical wound, despite intralesional curettage surgical technique.

We found that 42% of patients had significant complications associated with surgery and radiation therapy. Surgery for primary tumors of the spine carries a significant risk of morbidity. C1–2 chordomas have been reported to have a 71% risk of complications.⁴⁰ The authors of a series reviewing the complications of 220 en bloc spinal operations reported that 33% of their patients had major surgical complications, with those harboring primary malignant spinal tumors having a higher risk of complications.⁸ One study with long-term follow-up after proton radiotherapy for chordoma noted a Grade 3–4 toxicity risk of 13%.¹⁵ The surgical complication frequency of 18% reported in the present series, which included a delayed rod fracture 4 years after surgery, compares favorably with the surgical complication frequency reported in other series. Furthermore, none of our patients experienced the severe neurological and systemic complication reported after en bloc surgery. Among the radiation-associated complications currently reported, 2 patients had self-limited complications and only 1 patient had a persisting complication (vocal cord paralysis). Currently used esophageal dose constraints have resulted in a significantly decreased risk of esophageal toxicity.¹⁴

In the coming era, quality of life may become an increasing consideration in the treatment of chordoma, particularly in light of potentially effective adjuvant approaches on the horizon. A focus on targeted therapy including via receptor tyrosine kinase blockade as justified by the involvement of canonical oncological mechanisms, for example via the PI3K-AKT-mTOR and RAS-MAPK pathways, has yielded some promising early reports of response.^{1,11,16,24,47,51,53,54,56} Preclinical success with direct inhibition of the master transcription factor brachyury has led to optimism that this may be used as a therapeutic vulnerability clinically.²⁸ Additionally, interest in radiosensitization, vaccines, and immunotherapies, and with novel mechanistic insight from emerging from epigenetic discovery approaches, may potentially allow for future therapy abrogating the need for strategies emphasizing surgical cure via wide marginal excision.^{19,21,26,41,45,48}

Conclusions

Intralesional debulking and separation surgery followed by SBRT for chordoma of the mobile spine provides excellent local control for patients in whom aggressive en bloc resection with wide margins is not feasible. High-dose-per-fraction irradiation may provide biological benefits compared with conventional radiotherapy. Data from our series compare favorably with those in existing literature concerning local control.

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Dr. Yamada is a consultant for Varian Medical Systems and on the Speakers' Bureau of the Institute for Medical Education. Dr. Laufer receives consulting fees from DePuy/Synthes, SpineWave, and Globus. Dr. Bilsky receives consulting fees from DePuy/Synthes, Globus, and BrainLab. Dr. Lis reports being a consultant for Medtronic.

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Conception and design: Bilsky, Yamada, Schmitt, Laufer. Acquisition of data: Bilsky, DT Lockney, Shub, Hopkins, Lis, Yamada, Higginson. Analysis and interpretation of data: Bilsky, DT Lockney, Hopkins, NA Lockney, Lis, Schmitt, Higginson, Laufer. Drafting the article: DT Lockney, Hopkins, NA Lockney, Moussazadeh, Laufer. Critically revising the article: Bilsky, DT Lockney, Shub, Hopkins, NA Lockney, Moussazadeh, Schmitt, Laufer. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Bilsky. Statistical analysis: DT Lockney, NA Lockney, Laufer. Administrative/technical/material support: Bilsky. Study supervision: Bilsky, Laufer.

Supplemental Information

Videos

Video abstract. <https://vimeo.com/194713781>.

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