Focused resection of epidural disease followed by adjuvant spinal stereotactic radiosurgery is an effective palliative approach.

Separation Surgery for Spinal Metastases: Effect of Spinal Radiosurgery on Surgical Treatment Goals

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Background: The treatment of epidural spinal cord compression due to metastatic cancer represents an important clinical challenge. The NOMS (neurologic, oncologic, mechanical, and systemic) framework facilitates the determination of the optimal combination of systemic, radiation, and surgical therapies for individual patients. Spinal stereotactic radiosurgery (SRS) is an effective and safe modality for achieving durable control of local disease. Integrating SRS into the postoperative treatment plan allows surgical goals to be modified, thus decreasing the extent of tumor resection required.

Methods: Separation surgery is indicated for patients with spinal cord compression secondary to solid tumor metastases. During separation surgery, the spinal column is stabilized and the epidural tumor is resected without requiring significant vertebral body resection.

Results: Tumor separation from the spinal cord allows patients to undergo postoperative SRS.

Conclusions: The combination of separation surgery and high-dose hypofractionated or single-fraction SRS results in high local tumor control at 1 year and is an effective palliative paradigm for this patient population.

Multimodal Treatment for Metastatic Epidural Spinal Cord Compression

Spinal metastases occur in 30% to 40% of all patients with cancer.1,2 Certain cancers, such as prostate, breast, and melanoma, display osseous tropism, with more than one-half of patients with these cancers developing spinal metastases over the course of their illness.3 Metastatic disease in the spine leads to spinal instability, neurological deficits, and pain. Metastatic epidural spinal cord compression (ESCC) affects 5% to 10% of all patients with cancer and up to 40% of those with other bony metastases.4,6 Approximately 20,000 Americans present each year with spinal cord compression...
at the time of cancer diagnosis,7,8 with the Nationwide Inpatient Sample database reporting more than 8,000 annual admissions for malignant spinal cord compression.9 Symptom palliation represents the main treatment goal in these patients and is used to preserve or restore spinal stability and neurological function. As such, all local treatments must be planned to allow for the shortest interruption of systemic therapy.

Multimodal therapy is critical for the management of metastatic ESCC. In addition to medical treatment for the systemic burden of disease, numerous surgical and radiotherapeutic models have been employed. Historically, surgical approaches have included laminectomy without instrumented fusion, an approach largely abandoned due to the inability to resect ventral epidural and vertebral body disease, as well as the potential destabilization of the biomechanically vulnerable cancer spine with resultant pain and risk of neurological deterioration. With the improvement and popularization of spinal instrumentation, circumferential decompression requiring instrumented stabilization is frequently used. In a review of retrospective studies from 1964 to 2005, Witham et al10 demonstrated that adding laminectomy to radiation, as well as adding posterior stabilization to laminectomy and radiation, improved neurological function, with stable perioperative mortality rates among surgical series (36% vs 42% vs 64% mean improvements in neurological function). Although anterior decompression is associated with increased mean neurological improvement (75%), it is also associated with increased perioperative mortality (10% vs 5%–6% in the posterolateral series).10

In a randomized controlled study of surgical decompression with conventional radiotherapy (30 Gy in 10 fractions) compared with radiotherapy alone for metastatic ESCC secondary to solid malignancies, Patchell et al11 demonstrated superiority of a combined surgical and radiotherapeutic approach for the maintenance and recovery of ambulation, duration of ambulation, functional ability, maintenance of continence, and survival.

While surgery provides spinal stabilization and neural element decompression, radiation therapy provides local tumor control. Conventional external beam radiation therapy (cEBRT) has been the mainstay of spinal radiation for decades.12 Histology-specific sensitivity to cEBRT traditionally serves as the basis for the classification of tumors (radiosensitive vs radioresistant). cEBRT confers durable local control in radiosensitive metastatic pathologies, including hematological malignancies (lymphoma, plasmacytoma, multiple myeloma), small cell cancers, germ cell tumors, and breast and prostate carcinomas, with 2-year local control rates of 80% to 98%.13-16 However, most solid tumor metastases exhibit a spectrum of resistance to cEBRT, including tumors of renal, thyroid, hepatocellular, and colorectal origins, in addition to sarcoma and melanoma and, to a lesser extent, non–small-cell lung cancer. cEBRT conveyed 2-year control rates as low as 30% in gastrointestinal metastases, with a brief duration of motor improvement for bladder, lung, and kidney metastases, demonstrating durable improvements of 1 month, 4 months, and 5 months, respectively.17-20 Therefore, these tumor histologies were classified as radioresistant due to the unsatisfactory local control generally conferred by cEBRT. However, because spinal stereotactic radiosurgery (SRS) generally overcomes the resistance of these tumors to cEBRT — thus providing durable local control — the term “radioresistant” describes the relative resistance to cEBRT, rather than the overall outcome of radiation treatment.

High-dose hypofractionated radiotherapy using image-guided stereotactic techniques has largely overcome the radioresistance of spinal metastases that poorly respond to cEBRT. SRS delivers radiation to contoured target volumes with improved collateral tissue sparing, which is achieved via a steep dose gradient between target volumes and adjacent organs at risk. This technology is attractive for the treatment of spinal disease given the morbidity associated with local failure and the risk of toxicity associated with overdosing tissues in tumor proximity, including the spinal cord and esophagus. When treating spinal metastases without epidural extension, single-fractionated and multifractionated SRS each demonstrated 70% to 90% rates of durable local disease control, progression-free survival (PFS), and palliation as first-line therapy, re-treatment therapy, or both following failed cEBRT21-25; in the series by Gerszten et al,25 500 lesions were treated. One prospective report of radiosurgery for ESCC due to nonradiosensitive tumors (with eligible participants having a minimum of 4/5 lower extremity strength) describes a 65% mean reduction in epidural tumor volume at 2 months and an 81% rate of improvement in neurological function at 11.5 months of follow-up.24 However, of the 35 patients neurologically intact at presentation, the neurologic deterioration of 2 patients raised concerns about the safety and efficacy of SRS alone in patients with spinal cord compression.24 Two prospective studies demonstrated the safety and effectiveness of spinal SRS as first-line therapy for spinal metastasis in the absence of significant spinal cord compression.25,26 Furthermore, the conformal nature of radiation delivery decreases the radiation dose given to tissues surrounding the spine, allowing the delivery of SRS to previously radiated spinal regions.27-31 A meta-analysis of spinal reirradiation series yielded a median local control rate of 80% at 1 year (range: 66%–93%).52 Spinal toxicity, including myelopathy, paraparesis,
or both, is rare with post–cEBRT SRS salvage, with 1 prospective report describing a case of grade 3 lumbar plexopathy characterized as foot drop in addition to radicular pain and paresthesia.\textsuperscript{29} Sixty-three lesions were treated with either 30 Gy in 5 fractions or 27 Gy in 3 fractions and were followed-up for 17.6 months.\textsuperscript{29} Other series indicate that standard regimens impose no significant neurological toxicity: these series included 37 cases treated with a median dose of 24 Gy in 3 fractions, two-thirds of which were followed for at least 6 months\textsuperscript{27}; 79 cases treated with doses of 27 to 30 Gy in 3 fractions, with 15.9 months of follow-up\textsuperscript{33}; and 81 cases treated with 24 Gy in 3 fractions or 30 Gy in 5 to 6 fractions, with an overall survival rate of 11 months.\textsuperscript{31} One case-control study–based model suggested the safety of SRS reirradiation regimens, administered at least 5 months following cEBRT, delivering a maximal thecal sac normalized, biologically effective dose ($P_{\text{max \ nBED}}$) of 20 to 25 Gy (2/2) if the total $P_{\text{max \ nBED}}$ did not exceed 70 Gy (2/2) and the thecal sac SRS $P_{\text{max \ nBED}}$ was 50% or less of the total nBED.\textsuperscript{34}

The durable and reliable local control rates provided by cEBRT in spinal metastases sensitive to conventional fractionation and by SRS in cEBRT-resistant tumors have largely obviated the need for cytoreductive surgery in spinal metastases. Data indicate that the rate of local control following SRS is independent of tumor volume.\textsuperscript{35} Although cEBRT can be delivered, regardless of the degree of epidural tumor extension in radiosensitive tumors, SRS requires a separation of several millimeters between the tumor and the spinal cord to deliver tumoricidal radiation doses without risking radiation toxicity to the spinal cord. Therefore, the integration of radiation therapy into surgical planning has shifted the goal from maximal tumor resection surgery to separation surgery to provide a separation of the tumor from the spinal cord and to optimize the conditions for the safe and effective delivery of SRS.

### Patient Evaluation

The ESCC scale provides a common vocabulary to describe and stratify patients on the basis of the degree of epidural tumor extension.\textsuperscript{30} Tumors confined to bone (stage 0) and tumors with minor epidural extension without abutment or compression of the spinal cord (stages Ia and Ib) have the requisite separation from the spinal cord to be safely treated with SRS. These tumors are classified as low-grade ESCC. By contrast, tumors displacing or compressing the spinal cord (stages II and III, respectively) are classified as high-grade ESCC and require resection of the epidural component to separate the tumor from the spinal cord prior to SRS (Fig 1). The ESCC scale has good-to-excellent intra- and inter-rater reliability scores.

The ESCC scale represents 1 of the 4 considerations in the NOMS (neurological, oncological, mechanical, and systemic) algorithm (Fig 2). The NOMS framework allows the determination of the optimal combination and type of surgical, radiation and pharmacologic modalities for each patient by integrating neurological (N), oncological (O), mechanical (M), and systemic (S) considerations.\textsuperscript{37} The neurological consideration includes the degree of radiographic ESCC and a clinical determination of neurological symptomatology attributable to spinal cord or nerve root compression, while the oncological consideration relies on tumor histology to classify tumors into either radioresistant and radiosensitive pathology. Patients with radiosensitive tumors are generally treated with cEBRT regardless of ESCC, achieving good local control. By contrast, radioresistant tumors benefit from SRS for local control. Although patients with low-grade ESCC may undergo SRS without surgery, those with high-grade ESCC secondary to radioresistant tumors require separation surgery prior to SRS.

The mechanical consideration serves as an independent surgical indication. Patients with mechanical instability often require stabilization. The spinal

![ESCC scale](image-url)
column may be stabilized using open or percutaneously placed instrumentation in addition to cement augmentation. The Spinal Instability Neoplastic Score is a validated decision-making tool that facilitates the diagnosis of instability. Factors reflecting and governing stability — including tumor-level biomechanics (with increased instability with junctional or mobile spine disease over semirigid thoracic or rigid sacral involvement), the presence of pain, bony lysis, vertebral body collapse, posterolateral element involvement, or frank misalignment — are tallied and weighted to provide a score classified into stable, unstable, or indeterminate categories. For patients with an indeterminate or unstable score, surgical referral is indicated. Mechanical radiculopathy and the severe exacerbation of pain with recumbence or neck movement provide reliable symptoms of spinal instability. The comprehensive evaluation described in the NOMS algorithm also accounts for systemic tumor burden and any additional medical comorbidity affecting the expected survival of the patient and his or her tolerance for surgery.

**Separation Surgery**

The goals of separation surgery include epidural decompression and spinal stabilization without gross total or en bloc tumor resection. Generally, instrumented stabilization is performed prior to decompression in order to avoid the manipulation of hardware across an open spinal canal. Typically, pedicle or lateral mass screw-rod fixation is performed at a minimum of 2 levels superior and inferior to the level of decompression. Longer constructs or cement reinforcement of screw purchase may be required in patients with poor bone quality. Laminctomy is performed at the level of epidural tumor extension and at least partially above and below the levels of the tumor. Most of the bone removal is carried out using a 3-mm matchstick bur on a high-speed drill rather than a Kerrison punch to avoid iatrogenic injury. Tumor and ligamentous resections are performed using sharp dissection with a No. 15 blade and tenotomy scissors. The ligament resection is initiated at a tumor-free level so normal dural planes can be identified and the epidural tumor can be safely dissected.

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Fig 2. — The NOMS (neurological, oncological, mechanical, and systemic) algorithm for the treatment of spinal metastases. Radiosensitive malignancies are referred to conventional radiotherapy regardless of degree of cord compression. Radiosistant disease requires IMRT either upfront (in the absence of high-grade cord compression) or following decompressive separation surgery. Generally, IMRT is the chosen modality of adjuvant radiation for previously radiated tumors. Mechanical instability provides an independent surgical indication. cEBRT = conventional external-beam radiation, ESCC = epidural spinal cord compression, IMRT = intensity-modulated radiation therapy, SRS = stereotactic radiosurgery. Republished with permission of AlphaMed Press, from Laufer I, Rubin DG, Lis E, et al. The NOMS framework: approach to the treatment of spinal metastatic tumors. *Oncologist*. 2013;18(6):744-751; permission conveyed through Copyright Clearance Center, Inc.
To access the ventral epidural space, unilateral or bilateral facetectomy is performed followed by pedicle resection with a high-speed drill. This transpedicular approach allows the posterior longitudinal ligament and the ventral epidural tumor to be exposed without manipulation of the spinal cord. Following coagulation of the ventral epidural plexus, the posterior longitudinal ligament is resected to ensure complete dural decompression and to ventrally clear the dural margin. When dissecting the lateral dura, it is important to identify the exiting nerve roots, which are typically preserved during the dissection. When necessary for tumor resection, thoracic nerve roots below T1 are sacrificed. Two vascular clips are placed proximal to the dorsal root ganglion, which are then bipolar cauterized and ligated with tenotomy scissors. Partial corpectomy may be performed to facilitate decompression without aggressive attempts for gross total tumor or vertebral body resection. As a result, anterior constructs are rarely required. In cases with severe vertebral body destruction, anterior reconstruction may be carried out using polymethylmethacrylate with Steinmann pins; alternatively, polyether ether ketone or titanium cage placement can also be used with this posterolateral approach.41

**Stereotactic Radiosurgery**

Postoperative myelography is performed to delineate spinal cord and dural margins, as well as to avoid any radiographic artifact encountered on magnetic resonance imaging in the setting of proximate spinal instrumentation. The myelography and simulation are often performed prior to patient discharge from perioperative hospitalization. Single-fraction (24 Gy) or hypofractionated SRS (typically 18–36 Gy in 3–6 fractions) is administered.21,42 Individual fractionation regimens are prescribed on the basis of previous radiation, histological radiosensitivity, ESCC stage, paraspinal extension, and the number of spinal treatment levels. Typically, larger tumors (> 2 spine segments), epidural disease in excess of stage Ib ESCC, and cases of previous radiation are treated with high-dose hypofractionated regimens. High-dose single-fraction therapy is typically prescribed otherwise. For example, a 1- or 2-level tumor with stage Ia ESCC and no significant paraspinal tumor volume would likely be treated with a single fraction of 24 Gy. Alternatively, a 3-level tumor with stage Ib ESCC and esophageal abutment would likely be treated with a hypofractionated dose. Treatment plans may be affected by the use of intraoperative or percutaneous high-dose-rate brachytherapy, which allows conformal doses to the target lesion and improved critical-tissue sparing. Single-fraction SRS dose constraints in cases with no prior history of radiation are composed of a maximal spinal cord dose (as defined on myelography) of 14 Gy, an esophageal dose of 14.5 Gy, and a cauda equina dose of 16 Gy.

Gross tumor volume treatment contours are delineated on the basis of preoperative magnetic resonance imaging and include intrasosseous, epidural, and paraspinal disease, with radiation prescribed to the presurgical tumor extent, thus accounting for the decompressed postoperative dural margin demonstrated via myelography. Clinical tumor volumes are defined as extensions of the gross tumor volume to account for the presumed microscopic disease extension into adjacent marrow spaces (eg, the entire vertebral body when only a proportion of the body is radiographically involved).43 The planning treatment volume is a 2- to 3-mm expansion of the clinical tumor volume to
compensate for the small margin of error expected in the planning and delivery of radiation treatment. We generally administer postoperative SRS within 10 to 20 days of surgery, frequently prior to staple removal. A representative case is presented in Fig 3.

**Separation Surgery Plus Adjuvant Stereotactic Radiosurgery**

We recently described our experience with 186 patients (from 2002 to 2011) treated with decompressive separation surgery followed by adjuvant hypofractionated or high-dose single-fraction SRS. Among these patients, 136 exhibited high-grade cord compression (stage II or III ESCC) at presentation. Patients were treated with 1 to 8 levels of spinal decompression (median of 2 levels) followed by either low-dose per fraction (18–36 Gy in 5 or 6 fractions) hypofractionated SRS (58.6% of patients), high-dose per fraction (24–30 Gy in 3 fractions) hypofractionated SRS (19.9%), or 24 Gy single-fraction SRS (21.5%), with completion within a median of 1.6 months following surgery.

Postoperative SRS provided durable local control rates regardless of tumor histology. Overall, 18.3% of patients demonstrated local progression at a median of 4.8 months, 55.6% died without local progression at a median of 5.6 months, and the remaining 26.1% of patients were alive and without progression at the last follow-up (median of 7.1 months), with a cumulative local progression incidence of 16.4% at 1 year (95% confidence interval: 10.7–22.2; Fig 4). Univariate competing-risks analysis revealed the superiority of postoperative high-dose over low-dose hypofractionated SRS in PFS rates (95.9% vs 77.4%, respectively; hazard ratio [HR]: 0.12; \( P = .04 \)) and a trend toward superiority of single-fraction versus low-dose hypofractionated SRS (1-year PFS: 91.0%; HR: 0.45; \( P = .09 \)). The analysis failed to demonstrate an association between previous radiation or tumor histology with local control. These data provide evidence that high-dose per fraction SRS delivered either as single-fraction or hypofractionated treatments provide durable local control rates regardless of prior radiation or histology-intrinsic resistance to cEBRT.

In our experience, complications associated with separation surgery combined with adjuvant SRS are minimal. In our recent series, radiotherapy was not associated with any neurological morbidity, and 4 patients required repeat surgery for hardware failure (1 of whom had local progression). These data are in line with our previous findings of grade 1 skin reactions in 3 of 21 patients, 1 case of transient acute neuritic pain, 3 cases of grade 2 esophagitis, and 1 case of grade 4 esophagitis that required surgical repair of a fistula. Furthermore, in the most recent analysis of our 7-year experience, the overall rate of symptomatic hardware failure requiring reoperation following separation surgery in patients who did not have anterior reconstruction was 9 out of 318 patients (2.8%). Risk factors for failure included chest wall resection and initial construct length of 6 levels or more. SRS puts the treated vertebral bodies at risk for fracture when used as a stand-alone treatment. Postoperative vertebral body compression fractures within or adjacent to instrumented construct may be stabilized using percutaneous cement augmentation.

**Conclusions**

For patients with metastatic epidural spinal cord compression and high-grade spinal cord compression, separation surgery is a safe and effective treatment option. Although most spinal metastases can be successfully treated with conventional external-beam radiation or stereotactic radiosurgery depending on their...

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radiosensitivity, surgery remains indicated in cases of high-grade spinal cord compression in radioresistant or unknown malignancies. In this setting, focused resection of the epidural tumor via the posterolateral approach followed by adjuvant stereotactic radiosurgery provides durable, long-term local disease control regardless of prior radiation or tumor histology. Thus, integrating stereotactic radiosurgery into the treatment framework for spinal metastases may reduce the extent of tumor resection. Prospective studies of adjuvant radiotherapy timing and dosing are directed at outcome optimization with a minimization of late toxicity.

References