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Special Report

ACR Appropriateness Criteria® Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Expert Panel on Radiation Oncology–Bone Metastases:
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Abstract

Metastatic epidural spinal cord compression (MESCC) is an oncologic emergency and if left untreated, permanent paralysis will ensue. The treatment of MESCC is governed by disease, patient, and treatment factors. Patient's preferences and goals of care are to be weighed into the treatment plan. Ideally, a patient with MESCC is evaluated by an interdisciplinary team promptly to determine the urgency of the clinical scenario. Treatment recommendations must take into consideration the risk-benefit profiles of surgical intervention and radiotherapy for the particular individual's circumstance, including neurologic status, performance status, extent of epidural disease, stability of the spine, extra-spinal disease status, and life expectancy. In patients with high spinal instability neoplastic score (SINS) or retropulsion of bone fragments in the spinal canal, surgical intervention should be strongly considered. The rate of development of motor deficits from spinal cord compression may be a prognostic factor for ultimate functional outcome, and should be taken into account when a treatment recommendation is made. The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed every three years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer-reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of imaging and treatment procedures by the panel. In those instances where evidence is lacking or not definitive, expert opinion may be used to recommend imaging or treatment.

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The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Summary of Literature Review

Metastatic epidural spinal cord compression

The axial skeleton is a commonly involved site in patients with bone metastases. Progressive spinal metastasis may result in epidural spinal cord compression, and lead to paresis and paralysis if left untreated.[1–3] The treatment of metastatic epidural spinal cord compression is determined by disease factors such as histology, site of disease, extent of epidural disease, and extent of metastases elsewhere. Patient factors such as the neurologic status, Karnofsky Performance Status (KPS), and treatment factors, such as availability of qualified spine surgeon and advanced radiotherapy equipment, also have to be considered. Patient's preferences and goals of care are to be weighed into the treatment plan. Ideally, the patient with epidural spinal cord compression is evaluated by an interdisciplinary team including a combination of radiation oncologists, medical oncologists, spine surgeons, pain medicine specialists, interventional radiologists, physiatrists, and palliative care professionals in a timely fashion to determine the urgency of the clinical scenario.[1–3] Treatment recommendations must take into consideration the risk-benefit profiles of surgical intervention and radiotherapy for the particular individual's circumstance, including neurologic status, performance status, extent of epidural disease, stability of the spine, extra-spinal disease status, and life expectancy.[1–3] In patients with high spinal instability neoplastic score (SINS)[4] or retropulsion of bone fragments in the spinal canal, surgical intervention should be strongly considered. The rate of development of motor deficits from spinal cord compression may be a prognostic factor for ultimate functional outcome[5] and should be taken into account when a treatment recommendation is made.

The importance of a high index of suspicion in high-risk patients and a prompt diagnosis of metastatic spinal cord compression cannot be overemphasized.[1–3] The key goal of the treatment for metastatic epidural spinal cord compression is prompt decompression of the spinal cord in an attempt to prevent further deterioration of neurologic function or to reverse the neurologic deficits. This can be accomplished by surgical decompression with or without postoperative external beam radiotherapy (EBRT) or EBRT alone.[6] Systemic approaches such as chemotherapy, hormonal therapy, osteoclast inhibitors (OI), and radiopharmaceuticals, especially if given alone, are deemed not appropriate in this clinical scenario, since the goal of prompt decompression of the spinal cord is very unlikely to be achieved. Systemic therapy after appropriate local therapy for metastatic spinal cord compression may be appropriate for the treatment of systemic disease, depending on the clinical scenario. For most solid tumors, except radiosensitive and chemosensitive tumors such as hematologic tumors, germ cell tumors, and small cell carcinoma, there is level 1 evidence to suggest that surgical decompression followed by EBRT can yield superior functional outcomes compared to EBRT alone.[1–3] For patients who have poor performance status or are not otherwise suitable for surgical decompression, EBRT is regarded as a reasonable option. However, there is controversy as to the optimal dose schedules and fractionation that should be used.[7–13] For hematologic tumors such as lymphoma and plasma cell tumors/myeloma, EBRT alone is effective in the decompression of the spinal cord since those are radiosensitive tumors.[14,15]

Stereotactic body radiation therapy (SBRT) is an emerging therapy for spinal metastasis and has been used for the treatment of metastatic epidural spinal cord compression either as primary treatment, reirradiation treatment, or postoperative treatment,[16–20] with reasonable preliminary results based on some retrospective studies and a prospective study (reported only in abstract form)[19] with short-term follow-up. There are no comparative studies or randomized trials comparing EBRT and SBRT in these settings. More research is needed to better define the role of SBRT in metastatic spinal cord compression, either as primary treatment or in the postoperative setting.

Recurrent/progressive spinal metastasis after prior radiation therapy

With the improvement of systemic therapy, overall survival is improved in patients with metastatic cancer. As a result, it is more common to encounter scenarios where patients develop recurrent/progressive spinal metastases, sometimes causing spinal cord compression, after prior EBRT to the same index lesions. This presents a therapeutic challenge, since further EBRT will increase the risk of radiation myelopathy (RM), posing patient safety concerns. Data from a retrospective study showed that the risk of RM was zero after a biologically effective dose (BED) of ≤ 120 Gy_2 when the interval was not shorter than six months and the BED of each course was < 98 Gy_2.[21] However, due to the relatively small number of patients in these studies and the retrospective nature and relatively short follow-up periods of these studies, these datasets should be interpreted with caution.

As in metastatic epidural spinal cord compression, an interdisciplinary evaluation is crucial to determine the best treatment option for the patient. The ultimate treatment strategy is determined by disease factors such as histology, site of disease, extent of epidural disease, and extent of metastases elsewhere, patient factors such as the neurologic status and KPS, and treatment factors such as availability of spinal neurosurgeon and advanced radiotherapy equipment. If there is evidence of spinal instability or metastatic epidural spinal cord compression, surgical intervention should be strongly considered even when reirradiation is being considered. The patterns of progression of neurologic deficits from spinal cord compression may be predictive of ultimate functional outcome and should be taken into account when a treatment recommendation is made.[5] Patient's preferences and goals of care are to be weighed into the treatment plan.

SBRT can provide a means to effectively treat previously irradiated spinal metastases, while still being able to minimize the risk of RM, by adequately sparing the spinal cord.[22–24] Favorable outcomes and toxicity profiles have been reported after SBRT for recurrent/progressive spinal metastasis as sole or postoperative treatment.[20,22–25] However, all the studies are retrospective with a majority of them including patients treated for scenarios other than recurrent disease.[22–24,26,27] Furthermore, nearly all studies have relatively short follow-up, and studies comparing conventional strategies and SBRT

are very limited.[26,27] One of the biggest controversies is spinal cord tolerance for SBRT in the reirradiation setting and guidelines for practice have been defined to guide practice allowing the cumulative BED to reach 140 Gy_2 (normalized 2 Gy equivalent 70 $Gy_{2/2}$) with certain caveats, in particular, the SBRT component not exceeding 50 Gy_2 (normalized 2 Gy equivalent 25 $Gy_{2/2}$); however, more research is needed to better define the role of SBRT and to determine the spinal cord tolerance in the reirradiation setting.[28,29] Apart from surgical intervention with or without SBRT, SBRT alone, systemic approaches such as chemotherapy, hormonal therapy, OI, and radiopharmaceuticals are other treatment options, depending on the clinical scenario.

Variant 1

A 60-year-old man with stage IV non–small-cell lung cancer with KPS 80 and known asymptomatic spinal metastasis at T7 receives first line systemic therapy, then develops severe pain from the T7 metastasis (Brief Pain Inventory: 8 out of 10) associated with moderate epidural spinal cord compression leading to a gradual onset of sensory above the umbilicus and bilateral lower extremity weakness (motor power 4 out of 5). MRI of the thoracic spine shows no cerebrospinal fluid (CSF) around the mildly deformed cord at T7. PET/CT shows stable primary tumor in the lung and lung metastases. No bony retropulsion.

TABLES: ACR APPROPRIATENESS CRITERIA® METASTATIC EPIDURAL SPINAL CORD COMPRESSION AND RECURRENT SPINAL METASTASIS

Clinical condition: Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Variant 1: 60-year-old man with stage IV non–small-cell lung cancer with KPS 80 and known asymptomatic spinal metastasis at T7 received first line systemic therapy, then developed severe pain from the T7 metastasis (Brief Pain Inventory: 8 out of 10) associated with moderate epidural spinal cord compression leading to a gradual onset of sensory level above the umbilicus and bilateral lower extremity weakness (motor power 4 out of 5). MRI of the thoracic spine showed no CSF around the mildly deformed cord at T7. PET/CT showed stable primary tumor in the lung and lung metastases. No bony retropulsion.

Treatment	*Rating*[1]	*Comments*
Hospice after RT	3	
EBRT alone	5	
Systemic therapy and EBRT	5	
Systemic therapy and OI and EBRT	5	
Direct hospice placement	2	
Systemic therapy alone	2	
Systemic radiopharmaceuticals alone	2	
Surgical intervention alone	4	
Surgical intervention followed by EBRT	8	
Systemic therapy and OI	3	
SBRT alone	5	
Surgical intervention followed by SBRT	5	
EBRT dose		
8 Gy/1 fraction	5	
20 Gy/5 fractions	7	
30 Gy/10 fractions	8	
35 Gy/14 fractions	7	
40 Gy/20 fractions	4	
SBRT dose		
15–18 Gy/1 fraction	5	
20–24 Gy/2 fractions	5	
21–27 Gy/3 fractions	7	
20–30 Gy/5 fractions	7	
Treatment Planning		
CT simulation	8	
Fluoroscopic simulation	5	
Clinical simulation	4	
Posterior field only	5	
Anterior/posterior fields	7	
Posterior obliques	7	
SBRT (postoperative)	5	
IMRT	3	
Proton therapy to the bone metastasis	2	

[1]Rating scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.

CSF, cerebrospinal fluid; EBRT, external beam radiotherapy; IMRT, intensity-modulated radiation therapy; OI, osteoclast inhibitors; RM, radiation myelopathy; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

This is a case of spinal cord compression involving a spinal segment that has not been previously irradiated. Once spinal cord compression is confirmed, the patient should be started on corticosteroid and adequate analgesics promptly.[1–3] This patient has a good KPS and stable primary tumor and metastases in the lungs. The results of the multi-institutional phase III trial comparing surgical decompression and postoperative EBRT and EBRT alone for patients with metastatic epidural spinal cord compression can be applied to him.[6] Therefore, surgical intervention and postoperative EBRT can be considered, as this combination has been demonstrated to yield better functional outcomes compared to EBRT alone. The type of surgery to be offered, namely, separation surgery or more extensive decompression surgery such as vertebrectomy, is determined by judgment of clinical scenario including SINS,[4] and the experience and expertise of the treating center.

Surgical decompression also allows for prompt decompression of the spinal cord but should be followed with postoperative EBRT because of the substantial risk of recurrence. If a qualified spine surgeon is not available to perform a surgical decompression and a prompt transfer to a tertiary care center is not possible, radiotherapy in the form of EBRT alone may be considered but is considered to be suboptimal treatment.[1–3] Given the good KPS and stable extraspinal disease of the patient, hospice care alone may increase the risks of paralysis and/or progression if the patient lives long enough and the epidural spinal cord compression does not have local treatment. However, the patient may benefit from referral to palliative care/pain service for pain control along the course of his or her treatment. In the setting of primary EBRT, due to the presence of spinal cord compression, it is important to ascertain that the gross tumor is adequately treated.

Therefore, computed tomography (CT) simulation is commonly used provided that EBRT can be started promptly. If it is not possible to start EBRT promptly using CT planning or if CT simulation is not available, fluoroscopic simulation is regarded as a reasonable alternative. In the postoperative setting, the spinal cord is already decompressed and time is needed for healing of the surgical wound. As a result, prompt initiation of EBRT is not necessary. A CT simulation should be used to plan EBRT. Single-fraction EBRT delivering a dose of 8 Gy is deemed to be inadequate to prevent future recurrent spinal cord compression given the lower BED compared to multifraction EBRT, which can range from 20 Gy/5 fractions to 35 Gy/14 fractions. EBRT field arrangements, anterior/posterior (AP/PA), and PA alone are commonly used. Posterior oblique treatment approach can also be considered, as it is an easy, relatively conformal dosimetric approach that can reduce the volume of radiotherapy dose administered to the healed surgical wound and esophagus within the EBRT field. However, it can also result in higher lung dose. The treating physician will need to judge the risk and benefit of each technique on each individual patient.

SBRT has been used as primary treatment for metastatic epidural spinal cord compression from solid tumors causing mild neurologic deficits with favorable preliminary outcomes.[16,18,19] However, a very robust infrastructure is required for the prompt execution of the SBRT process to facilitate prompt initiation of treatment of this emergent condition, and this is only possible in very few treatment centers. Furthermore, it is unclear whether the long-term outcomes are comparable to those achieved with surgical intervention and postoperative EBRT or EBRT alone given the need to underdose the portion of the spinal metastasis abutting the spinal cord to avoid RM. In the postoperative setting, if adequate resection of the epidural disease is achieved, thereby creating a gap between the spinal metastasis and the spinal cord, SBRT may be considered, although more data and longer follow-up are required in order to establish this as one of the standard postoperative treatment options.[17,20]

There is even more-limited data on the use of intensity-modulated radiation therapy (IMRT) or proton beam therapy for primary or postoperative treatment of metastatic epidural spinal cord compression, and these modalities are best tested in a clinical trial setting. Systemic radiopharmaceuticals and osteoclast inhibition are not expected to decompress the spinal cord compression. Although one study shows that systemic OI may improve control of metastatic epidural spinal cord compression,[30] there is no conclusive evidence it is helpful in this setting, and should not be considered a specific therapy for existing spinal cord compression. Given the fact that the patient has progressive disease in T7 and has only had first line chemotherapy, further systemic therapy may be considered (see Variant 1 table).

Variant 2

A 65-year-old woman with known multiple myeloma but with no prior therapy develops gradual onset of a sensory level in the lower chest and moderate bilateral lower-extremity weakness (motor power 3 out of 5) over one week from an epidural spinal cord compression at T5. There is associated moderate pain (Brief Pain Inventory: 6 of 10). MRI shows circumferential compression of the spinal cord by myeloma. There is no evidence of vertebral compression fracture. KPS is 70. Skeletal survey reveals several other sites of asymptomatic lytic metastases throughout the axial and appendicular skeleton.

This patient without a history of prior therapy presents with extensive epidural spinal cord compression at T5 from myeloma. The main goals of treatment are to decompress the spinal cord and to control the pain. Steroid therapy should be started promptly to decrease cord edema/inflammation and it also has therapeutic effect against myeloma.[15] Since plasma cell tumors are very radiosensitive even to a low to moderate dose of radiation, the most commonly offered treatment is emergent EBRT after initiation of steroid therapy.[3,15] Adding OI to the treatment of multiple myeloma reduces pathologic vertebral fractures and pain, and it can be considered in conjunction with EBRT.[31] In light of the slight risk of osteonecrosis of the jaw associated with OI administration, a pretreatment dental evaluation to assess dentition and potential risk prior to starting OI might be necessary. OI with pamidronate or zoledronic acid are FDA approved for use in multiple myeloma, but not denosumab. Surgical intervention is generally not required unless present or impending spinal instability is contributing to the cord compression and SINS can provide guidance.[4]

Kyphoplasty is not indicated for this patient, since it is usually considered for pathologic vertebral compression fractures and is usually not offered in the setting of spinal

Clinical condition: Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Variant 2: 65-year-old woman with known multiple myeloma but with no prior therapy develops gradual onset of a sensory level in the lower chest and moderate bilateral lower-extremity weakness (motor power 3 out of 5) over one week from an epidural spinal cord compression at T5. There is associated moderate pain (Brief Pain Inventory: 6 of 10). MRI shows circumferential compression of the spinal cord by myeloma. There is no evidence of vertebral compression fracture. KPS is 70. Skeletal survey reveals several other sites of asymptomatic lytic metastases throughout the axial and appendicular skeleton.

Treatment	*Rating*[1]	*Comments*
Steroid therapy and EBRT, followed by OI and chemotherapy	8	
Steroid therapy and EBRT, followed by chemotherapy	8	
Steroid therapy and EBRT, followed by OI	6	
Steroid therapy and EBRT	6	
Steroid therapy and OI and chemotherapy	3	
Steroid therapy and chemotherapy	3	
Steroid therapy and OI	3	
EBRT alone	5	
Steroid therapy alone	3	
OI alone	2	
Hospice after EBRT	3	
Observation	1	
Surgical decompression alone	3	
Surgical decompression, followed by EBRT	3	
SBRT alone	2	
Surgical decompression, followed by SBRT	2	
Systemic radiopharmaceuticals alone	2	
Direct hospice placement	2	
EBRT dose		
8 Gy/1 fraction	4	
20 Gy/5 fractions	6	
20 Gy/10 fractions	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
30 Gy/10 fractions	8	
35 Gy/14 fractions	7	
40 Gy/20 fractions	4	
Treatment planning		
CT simulation	8	
Fluoroscopic simulation	7	
Clinical simulation	4	
Posterior field only	6	
Anterior/posterior fields	7	
Posterior obliques	7	
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	2	

[1]Rating scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.

CSF, cerebrospinal fluid; EBRT, external beam radiotherapy; IMRT, intensity-modulated radiation therapy; OI, osteoclast inhibitors; RM, radiation myelopathy; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

cord compression.[32] Systemic treatment should be considered given the presence of systemic disease and her reasonably good performance status. While there are no definitive data to suggest the most appropriate RT dose, fractionation schedules ranging from a single 8 Gy fraction to 40 Gy/20 fractions are all commonly used. Given the fact that the patient is relatively young and has reasonable performance status and a good chance of having neurologic improvement after EBRT,[5] more fractionated regimens, such as 30 Gy/10 fractions or 35 Gy/14 fractions, delivering a higher BED, are favored.[14] CT simulation to accurately include the involved vertebrae and account for body habitus in EBRT dose calculation is most desirable. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA, PA alone, and posterior obliques are commonly used. A posterior oblique treatment approach may be favored over an AP/PA or PA beam arrangement, as it is an easy, relatively conformal dosimetric approach that can reduce the dose administered to the skin, and this may be beneficial if spinal surgery may come into play in the later course of the disease. However, it can also result in higher lung dose.

The treating physician will need to judge the risk and benefit of each technique in each individual patient. The use of more sophisticated highly conformal approaches like SBRT, IMRT, and protons—all of which are very labor intensive in the treatment planning process—in an aim to escalate the radiation dose to a very radiosensitive tumor in an emergent setting, is considered insufficiently studied[3] (see Variant 2 table).

Variant 3

A 75-year-old woman with known progressive metastatic colon cancer resistant to two lines of systemic therapy develops increased pain in the middle back and sudden onset of total paralysis of bilateral lower extremity one week prior to admission to hospital from a nursing home. Her KPS is 50. The pain is rated 7 out of 10 on the Brief Pain Inventory. The lower extremity power is 0 out of 5 and the sensory level is located above the umbilicus. MRI of the spine shows diffuse spinal metastasis and circumferential compression of the spinal cord at T8 from bulky metastasis with no surrounding CSF. She has no prior history of EBRT to T8. The CT scan shows diffuse lung and liver metastases.

This is a case of established spinal cord compression at a spinal level that has not been previously irradiated. This patient developed sudden onset of total paralysis of bilateral lower extremity one week prior to presenting to the radiation oncologist. Data in the literature show that patients with sudden onset of total paralysis of extremities from metastatic epidural spinal cord compression are much less likely to regain function after treatment.[5] Furthermore, there is a delay of one week, rendering functional recovery extremely unlikely. The patient also has very poor KPS and has uncontrolled systemic disease after two lines of systemic chemotherapy. The life expectancy is short. All the above factors render an aggressive approach such as surgical decompression futile.

The only goal of treatment in this case is pain control with no potential for functional recovery. Medications to aid symptom control may include steroids and analgesics. Steroid therapy, preferably high dose, is typically used in managing severe spinal cord compression.[3] EBRT is very

Clinical condition: Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Variant 3: 75-year-old woman with known progressive metastatic colon cancer resistant to two lines of systemic therapy develops increased pain in the middle back and sudden onset of total paralysis of bilateral lower extremity one week prior to admission to hospital from a nursing home. Her KPS is 50. The pain is rated 7 out of 10 on Brief Pain Inventory. The lower extremity power is 0 out of 5 and the sensory level is located above the umbilicus. MRI of the spine shows diffuse spinal metastasis and circumferential compression of the spinal cord at T8 from bulky metastasis with no surrounding CSF. She has no prior history of EBRT to T8. CT scan shows diffuse lung and liver metastases.

Treatment	*Rating*[1]	*Comments*
Hospice after EBRT	8	
EBRT alone	7	
Direct hospice placement	6	
Chemotherapy and EBRT	3	
Chemotherapy and OI and EBRT	3	
Chemotherapy alone	2	
Systemic radiopharmaceuticals alone	2	
Surgical intervention alone	2	
Chemotherapy and OI	2	
SBRT alone	2	
EBRT dose		
8 Gy/1 fraction	7	
20 Gy/5 fractions	7	
30 Gy/10 fractions	5	
35 Gy/14 fractions	4	
40 Gy/20 fractions	3	
Treatment planning		
CT simulation	8	
Fluoroscopic simulation	7	
Clinical simulation	5	
Posterior field only	7	
Anterior/posterior fields	7	
Posterior obliques	7	
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	1	

[1]Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.

CSF, cerebrospinal fluid; EBRT, external beam radiotherapy; IMRT, intensity-modulated radiation therapy; OI, osteoclast inhibitors; RM, radiation myelopathy; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

effective for pain control. Direct hospice placement can be considered if pain can be adequately controlled by medications. Hospice placement after EBRT is also reasonable to avoid the logistic difficulties of coming to the radiation center for EBRT, although some hospices accommodate palliative EBRT.[33]

Systemic radiopharmaceuticals, chemotherapy, or OI are unlikely to offer benefit in a patient with very limited lifespan and spinal cord compression. Due to the spinal cord compression and the bulk of disease, CT simulation and EBRT are a reasonable approach. Given the poor prognosis, a single dose of 8 Gy may be considered as 20 Gy/5 fractions and 30 Gy/10 fractions, and longer fractionation regimens such as 35 Gy/14 fractions and 40 Gy/20 fractions may not offer extra benefit, since long-term toxicities are not an active concern in this case. Fluoroscopic simulation is regarded as a reasonable alternative. Clinical simulation, defined as setting up of a patient at the treatment machine without kilovoltage films, is usually not preferred. Common EBRT field arrangements, AP/PA, PA, and posterior obliques alone, are commonly used. Highly conformal approaches like SBRT, IMRT, and protons may not offer extra benefit given the expected poor prognosis, the need for prompt treatment, and the limited data on these approaches in this setting. Surgical intervention is usually not offered in this setting due to the expected poor prognosis, the limited life expectancy, and diffuse extent of disease[3] (see Variant 3 table).

Variant 4

A 45-year-old man with known metastatic renal cell carcinoma develops increased pain in the lower back. He has received sunitinib for his systemic disease. His KPS is 80. The pain is rated 8 out of 10 on the Brief Pain Inventory. There are no associated sensory or motor deficits in the lower extremities. He has a history of palliative EBRT to spinal levels T12–L2 to a dose of 30 Gy in 10 fractions one year prior to this presentation. MRI shows progression of spinal metastasis at L1 vertebral body, and there is no epidural extension or vertebral compression fracture. CT scan shows that the lungs are the only other organs with metastatic renal cell carcinoma and they have demonstrated good response to sunitinib.

The patient's systemic disease appears to be stable otherwise, and his KPS is 80. The recurrent spinal metastasis at the L1 vertebral body is the only symptomatic site of disease. Given the controlled extraspinal systemic disease and the good performance status, the survival of this patient can potentially extend beyond six months.

As a result, active treatment of the symptomatic lesion, which will entail reirradiation of the spine, is indicated to control his symptoms and to avoid further progression that may lead to spinal cord compression. Reirradiation with EBRT using conventional techniques poses an increased risk of RM should the patient's survival time exceed six months. Means to treat this symptomatic L1 lesion include surgical intervention, reirradiation with advanced radiation techniques, or systemic anticancer interventions with drug therapy or radiopharmaceuticals. Steroids, OI, and analgesics may improve pain control and should be considered. Surgery may be considered if there is spinal instability based on SINS, if the adjacent, irradiated bone appears stable, and the patient's life expectancy is >3–6 months, and if there is appropriate surgical expertise to extirpate the recurrent L1 vertebral body metastasis if surgery is indicated. The decision to proceed with surgery in this situation is very nuanced; patients with involvement of the vertebral body and posterior elements, other evidence of spinal instability, or refractory symptoms may benefit from surgical intervention if their performance status allows. Patients with higher SINS may benefit from vertebrectomy followed by stabilization.[4] Surgery can provide rapid relief of debilitating pain and may be considered given the patient's good performance status. There is a fair amount of information to provide guidance for reirradiation of spinal metastases.[22–24,26,27]

Goals of treatment include prevention of further progression of spinal metastasis and providing pain relief while minimizing the risk of RM. Highly conformal techniques like proton therapy, SBRT, or IMRT should be considered if appropriate expertise and equipment are available and if sustained positioning is achievable for the patient. Ideally, the patient can be enrolled in a clinical trial, if one is available. Different fractionation regimens have been used in SBRT for reirradiation of recurrent spinal metastasis, and they are all achievable provided the cord tolerance could be respected. There are some studies analyzing spinal cord tolerance in the reirradiation setting based on real patient data using linear-quadratic (LQ)[29] and generalized LQ models.[28] The data obtained from those analyses are yet to be validated further. Since there is no spinal canal involvement in this case, systemic therapies, including radiopharmaceuticals, could be given either as an adjuvant therapy or alone if surgery is not indicated and if pain can be controlled with analgesics. He will likely benefit from further systemic drug therapy after his recurrent spinal metastasis is treated, given the previous good response of his extraspinal disease to systemic drug therapy and his good performance status (see Variant 4 table).

Variant 5

A 56-year-old postmenopausal woman with known metastatic breast carcinoma, estrogen and progesterone receptors and HER2 positive, develops increased pain in the upper back and gradual onset of bilateral lower extremity weakness (motor power 4+ out of 5) over more than two weeks. Her KPS is 80. The pain is rated 7 out of 10 on the Brief Pain Inventory. She has a history of palliative EBRT to spinal levels T2–T6 to a dose of 30 Gy in 10 fractions two years prior to this presentation. MRI shows progression of spinal metastasis at T4, and there is epidural extension from the vertebral body and left pedicle, compressing on the spinal cord with no CSF surrounding the cord. There is no associated vertebral compression fracture. She has received two lines of systemic therapy with stable metastatic disease in the lungs and in multiple sites in the bones apart from the T4 vertebra on PET/CT.

This patient presents with epidural spinal cord compression from breast cancer in a previously irradiated spinal segment. The main goals of treatment are reversal of neurologic deficit, prevention of further progression of neurologic

Clinical condition: Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Variant 4: 45-year-old man with known metastatic renal cell carcinoma develops increased pain in the lower back. He has received sunitinib for his systemic disease. His KPS is 80. The pain is rated 8 out of 10 on Brief Pain Inventory. There are no associated sensory or motor deficits in the lower extremities. He has a history of palliative EBRT to spinal levels T12–L2 to a dose of 30 Gy in 10 fractions one year prior to this presentation. MRI shows progression of spinal metastasis at L1 vertebral body and there is no epidural extension or vertebral compression fracture. CT scan shows that the lungs are the only other organs with metastatic renal cell carcinoma and they have demonstrated good response to sunitinib.

Treatment	*Rating*[1]	*Comments*
Surgical intervention alone	5	
EBRT alone	3	
Surgical intervention and EBRT	3	
Surgical intervention and EBRT and systemic radiopharmaceuticals	3	
Systemic therapy, surgical intervention and EBRT	3	
Systemic therapy and EBRT	3	
SBRT alone	7	
Surgical intervention and SBRT	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
Surgical intervention and SBRT and systemic radiopharmaceuticals	3	
Systemic therapy, surgical intervention and SBRT	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
Systemic therapy and SBRT	7	
Systemic therapy and surgical intervention	6	
Surgical intervention and systemic radiopharmaceuticals	4	
Hospice after treatment (surgery or SBRT) of the spine	3	
Systemic radiopharmaceuticals alone	2	
Direct hospice placement	2	
Systemic therapy alone	2	
OI alone	2	
EBRT dose		
8 Gy/1 fraction	3	
20 Gy/5 fractions	3	
20 Gy/8 fractions	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
25 Gy/10 fractions	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
30 Gy/10 fractions	3	
35 Gy/14 fractions	3	
40 Gy/20 fractions	2	
SBRT dose		
15–18 Gy/1 fraction	7	
20–24 Gy/2 fractions	7	
21–27 Gy/3 fractions	7	
25–40 Gy/5 fractions	7	
Treatment planning		
CT simulation	9	
Fluoroscopic simulation	4	
Clinical simulation	2	
Posterior field only	2	
Anterior/posterior fields	3	
Posterior obliques	4	
SBRT	8	
IMRT	7	
Proton therapy to the bone metastasis	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.

[1]Rating scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.

CSF, cerebrospinal fluid; EBRT, external beam radiotherapy; IMRT, intensity-modulated radiation therapy; OI, osteoclast inhibitors; RM, radiation myelopathy; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

Clinical condition: Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis

Variant 5: 56-year-old postmenopausal woman with known metastatic breast carcinoma, estrogen and progesterone receptors, and HER2 positive develops increased pain in the upper back and gradual onset of bilateral lower extremity weakness (motor power 4+ out of 5) over more than two weeks. Her KPS is 80. The pain is rated 7 out of 10 on Brief Pain Inventory. She has a history of palliative EBRT to spinal levels T2–T6 to a dose of 30 Gy in 10 fractions two years prior to this presentation. MRI shows progression of spinal metastasis at T4 and there is epidural extension from the vertebral body and left pedicle, compressing on the spinal cord with no CSF surrounding the cord. There is no associated vertebral compression fracture. She has received two lines of systemic therapy with stable metastatic disease in the lungs and in multiple sites in the bones apart from the T4 vertebra on PET/CT.

Treatment	*Rating*[1]	*Comments*
Surgical intervention alone	5	
EBRT alone	3	
Surgical intervention and EBRT	5	
Surgical intervention and EBRT and systemic radiopharmaceuticals	4	
Systemic therapy, surgical intervention and EBRT	4	
Systemic therapy and EBRT	3	
SBRT alone	5	
Surgical intervention and SBRT	7	
Surgical intervention and SBRT and systemic radiopharmaceuticals	5	
Systemic therapy, surgical intervention and SBRT	8	
Systemic therapy and SBRT	5	
Systemic therapy and surgical intervention	5	
Surgical intervention and systemic radiopharmaceuticals	4	
Hospice after treatment (surgery or SBRT) of the spine	3	
Systemic radiopharmaceuticals alone	2	
Direct hospice placement	2	
Systemic therapy alone	2	
OI alone	2	
EBRT dose		
8 Gy/1 fraction	3	
20 Gy/5 fractions	3	
20 Gy/8 fractions	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
25 Gy/10 fractions	5	This treatment may be appropriate but there was disagreement among panel members on the appropriateness rating as defined by the panel's median rating.
30 Gy/10 fractions	3	
35 Gy/14 fractions	3	
40 Gy/20 fractions	3	
SBRT dose		
15–18 Gy/1 fraction	7	
20–24 Gy/2 fractions	7	
21–27 Gy/3 fractions	7	
25–40 Gy/5 fractions	7	
Treatment planning		
CT simulation	9	
Fluoroscopic simulation	4	
Clinical simulation	2	
Posterior field only	3	
Anterior/posterior fields	4	
Posterior obliques	4	
SBRT	7	
IMRT	7	
Proton therapy to the bone metastasis	2	

[1]Rating scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.

CSF, cerebrospinal fluid; EBRT, external beam radiotherapy; IMRT, intensity-modulated radiation therapy; OI, osteoclast inhibitors; RM, radiation myelopathy; RT, radiation therapy; SBRT, stereotactic body radiation therapy.

deficits, and pain control. Given her good performance status and potential for further systemic therapy, her lifespan is expected to be longer than 6 to 12 months. Although a cure is not anticipated, preservation of her lower extremity neurologic function and good pain control during her anticipated prolonged survival period is crucial to the patient. The gradual progression of her neurologic deficit over more than two weeks and her fairly good current lower extremity strength suggest that with decompression of the spinal cord there is a good possibility of regaining her lower extremity strength to nearly its full extent and maintaining a good ambulatory function.[5]

Prompt initiation of steroid therapy is indicated. A prompt decompression of the spinal cord is crucial in the determination of the eventual neurologic outcome. In light of her previous EBRT to the same region, further EBRT delivering an efficacious dose to the site of spinal cord compression using conventional techniques will result in an increased risk of RM, especially when the patient is expected to have a potentially long survival. Surgical decompression should be offered in this situation given its ability to rapidly decompress the spinal cord and the increased risk of RM resulting from reirradiation with the conventional EBRT option. The type of surgery to be offered, namely separation surgery or more extensive decompression surgery such as vertebrectomy, is determined by judgment of the clinical scenario including SINS,[4] and the experience and expertise of the treating center. After surgical decompression, close observation or postoperative SBRT,[17,20] if the expertise and equipment are available, may be considered.

There is some data in the literature on postoperative SBRT in the reirradiation setting and promising results have been observed.[17,20] However, comparative studies and randomized trials are lacking. There is also concern over RM, although the reported incidence is very low even in the reirradiation setting. Different fractionation regimens have been used in SBRT for reirradiation of recurrent spinal metastasis, and they are all achievable provided the cord tolerance could be respected. There are some studies analyzing spinal cord tolerance in the reirradiation setting based on real patient data using LQ[29] and generalized LQ models.[28] The data obtained from those analyses are yet to be validated further. SBRT has been used as primary treatment for reirradiation of metastatic epidural spinal cord compression from solid tumors, causing mild neurologic deficits.[19] However, the data is very limited in terms of efficacy and safety, particularly in the setting of reirradiation. Furthermore, a very robust infrastructure is required for the prompt execution of the SBRT process to facilitate prompt initiation of treatment of this emergent condition, and this is only possible in very few treatment centers. This modality is best considered in a clinical trial in this setting. Systemic radiopharmaceuticals are unlikely to be an effective decompressive treatment in this setting. Although one study shows that systemic OI may improve control of metastatic epidural spinal cord compression,[30] there is no conclusive evidence it is helpful in this setting, and it should not be considered a specific therapy for existing spinal cord compression. Given the fact that the patient has progressive disease in T4 and has only had two lines of systemic therapy, further systemic therapy may be considered (see Variant 5 table).

Summary of Recommendations

- Metastatic epidural spinal cord compression will lead to paresis and paralysis if left untreated and is an oncologic emergency.
- The aim of treatment is to provide prompt decompression of the spinal cord to avoid neurologic deterioration or to recover some neurologic function.
- Treatment recommendations must take into consideration the risk-benefit profiles of surgical intervention and radiotherapy for the particular individual's circumstance.
- The rate of development of motor deficits from spinal cord compression may be a prognostic factor for ultimate functional status and should be taken into account when a treatment recommendation is made.
- There is level 1 evidence to suggest that surgical decompression followed by external beam radiotherapy (EBRT) can yield superior functional outcomes compared to EBRT alone.
- EBRT is regarded as a reasonable option for patients with poor performance status or who are unsuitable candidates for decompression surgery.
- Stereotactic body radiotherapy (SBRT) has been used as primary treatment for metastatic epidural spinal cord compression from solid tumors causing mild neurologic deficits with favorable preliminary outcomes, but there is a risk of further neurologic deterioration during the planning of this very labor-intensive procedure.
- SBRT has also been used as adjuvant treatment after surgical decompression with favorable preliminary outcomes and may be appropriate in patients with adequate resection of the epidural disease, although more data is required in order to establish this as one of the standard postoperative treatment options.
- Recurrent/progressive spinal metastases in spinal segments that have received prior EBRT present a therapeutic challenge, since further EBRT will increase the risk of radiation myelopathy (RM).
- If there is evidence of spinal instability or metastatic epidural spinal cord compression, surgical intervention should be strongly considered even when reirradiation is being considered.
- SBRT as a primary or postoperative treatment can provide a means to effectively treat previously irradiated spinal metastases, while still being able to minimize the risk of RM, by adequately sparing the spinal cord, with favorable outcomes and toxicity profiles reported.
- Nearly all studies on SBRT for recurrent/ progressive spinal metastases have relatively short follow-up, and studies comparing conventional strategies and SBRT are very limited.
- There are limited studies analyzing spinal cord tolerance for SBRT in the reirradiation setting using individual patient data, but they are subject to further rigorous clinical validation.

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