JOURNAL OF PALLIATIVE MEDICINE
Volume 16, Number 1, 2013
DOI: 10.1089/jpm.2012.0376

Special Report

ACR Appropriateness Criteria® Spinal Bone Metastases

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Abstract

The spine is a common site of involvement in patients with bone metastases. Apart from pain, hypercalcemia, and pathologic fracture, progressive tumor can result in neurologic deterioration caused by spinal cord compression or cauda equina involvement. The treatment of spinal bone metastases depends on histology, site of disease, extent of epidural disease, extent of metastases elsewhere, and neurologic status. Treatment recommendations must weigh the risk-benefit profile of external beam radiation therapy (EBRT) for the particular individual's circumstance, including neurologic status, performance status, extent of spinal disease, stability of the spine, extra-spinal disease status, and life expectancy. Patients with spinal instability should be evaluated for surgical intervention. Research studies are needed that evaluate the combination or sequencing of localized therapies with systemic therapies including chemotherapy, hormonal therapy (HT), osteoclast inhibitors (OI), and radiopharmaceuticals. The roles of stereotactic body radiation therapy (SBRT) in the management of spinal oligometastasis, radioresistant spinal metastasis, and previously irradiated but progressive spinal metastasis are emerging, but more research is needed to validate the findings from retrospective studies. The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed every 2 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.

Summary of Literature Review

Introduction/Background

The axial skeleton is a common site of involvement in patients with bone metastases. Apart from pain, hypercalcemia, and pathologic fracture, progressive tumor can result in neurologic deterioration caused by spinal cord compression or cauda equina involvement. The treatment of spinal bone metastases depends on many factors including histology, site of disease, extent of epidural disease, extent of metastases elsewhere, and neurologic status. Ideally, patients with spinal bone metastases are evaluated by an interdisciplinary team including a combination of radiation oncologists, medical oncologists, spine surgeons, pain medicine specialists, interventional radiologists, psychiatrists, and palliative care professionals. Treatment recommendations must weigh the risk-benefit profile of radiation therapy (RT) for the particular individual's circumstance, including

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Accepted August 22, 2012.

neurologic status, performance status, extent of spinal disease, stability of the spine, extra-spinal disease status, and life expectancy. Patients with spinal instability should be evaluated for surgical intervention.[1] Research studies are needed that evaluate the combination or sequencing of localized therapies such as surgery and external beam radiotherapy (EBRT) with systemic therapies including chemotherapy, hormonal therapy (HT), osteoclast inhibitors (OI), and radiopharmaceuticals.[2–4]

Under current practice, systemic chemotherapy and/or HT and OI are frequently administered when asymptomatic bone metastases are first diagnosed. EBRT is usually delayed until the metastatic disease progresses and causes significant pain or creates a risk for pathologic fracture or spinal cord compression. The use of radiopharmaceuticals is generally considered in a small fraction of patients with persistent multifocal sites of pain or recurrence of pain in a previously irradiated site.[5]

Stereotactic body radiation therapy (SBRT) is an emerging therapy for spinal metastasis as primary treatment, postoperative treatment, or salvage treatment after prior EBRT or spinal cord compression.[6,7] Preliminary results based on retrospective studies and a small number of prospective studies appear to be promising, but the follow-up intervals for most studies are short and the reported endpoints are not uniform, rendering comparison with other conventional therapies difficult. A limited number of prospective studies and clinical trials show promising results.[6,8] SBRT's roles in the management of spinal oligometastasis, radioresistant spinal metastasis, and previously irradiated but progressive spinal metastasis are emerging, but more research is needed to validate the findings from retrospective studies. Logistically, the treatment planning and delivery processes require much more time and resources.

Epidural spinal cord compression represents a special situation for treating spinal metastasis and is an oncologic emergency.[9] The key goal of the treatment is prompt decompression of the spinal cord in order to prevent further deterioration of neurologic function or to reverse the neurologic deficits. This can be accomplished by surgical decompression or EBRT.[9] For most solid tumors, except radio- and chemo-sensitive tumors such as germ cell tumors and small-cell carcinomas, surgical decompression followed by EBRT has been demonstrated to yield superior functional outcomes compared with EBRT alone.[10,11] For patients who have poor performance status or are not suitable for surgery, EBRT is regarded as a reasonable option, although there is some debate as to optimal dose schedules and fractionation.[9,12] Hematologic tumors such as lymphoma and plasma cell tumors/myeloma are radiosensitive, and EBRT alone is effective in decompressing the spinal cord. SBRT has been used to decompress spinal cord compression, but data in the literature are limited.[12,13] More research is needed to define its role in managing spinal cord compression.

Variant 1 Discussion

This is a case of spinal cord compromise involving a region that has not been previously irradiated. This patient is expected to have very poor prognosis, and local palliative EBRT to prevent lower-extremity paralysis before referral for hospice care is regarded as the most appropriate treatment plan. Medications to aid symptom control may include steroids and analgesics. Moderate- to high-dose steroids are typically used in managing spinal cord involvement. Hospice placement after EBRT is favored to avoid the logistic difficulties of coming to the radiation center for EBRT, although some hospices accommodate palliative EBRT.[14]

Due to the spinal cord compression and the bulk of disease with paraspinous involvement, computed tomography (CT) simulation and EBRT are recommended, ranging from a single 8 Gy fraction to 30 Gy10 fractions. Given the poor prognosis, a single dose of 8 Gy is deemed as appropriate as 20 Gy in 5 fractions and 30 Gy in 10 fractions, and longer fractionation regimens such as 35 Gy in 14 fractions and 40 Gy in 20 fractions are deemed not to be appropriate because long-term toxicities are not an active concern in this case.[15–17] 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, anterior/posterior (AP/PA), PA and posterior obliques alone, are considered appropriate. Highly conformal approaches such as SBRT, intensity-modulated radiation therapy (IMRT), and protons are considered inappropriate given the expected poor prognosis, the need for prompt treatment, the numerous levels involved, and the limited data on these approaches.[18] Surgical intervention is not considered appropriate due to the expected poor prognosis, the multiple vertebral levels involved, and the limited life expectancy. There are concerns regarding the futility of administering further chemotherapy, given the prior treatment history and the extent of tumor burden, although the patient may be considered for an experimental protocol if it is available and the patient is deemed eligible.[19,20] (See Table 1.)

Variant 2 Discussion

There is a localized symptomatic region of bone metastases. This patient has a fairly good performance status and vertebral involvement. She has incurable disease, and the goals of care are palliative. The use of EBRT with analgesics, initiation of HT, and OI,[21] is regarded as the most appropriate treatment. HT, like localized RT, incurs limited morbidity while treating symptomatic disease and limiting consequential disease progression.[22] The use of RT to control pain and tumor burden constitutes a skeletal-related event (SRE). This scenario warrants the use of an OI to further reduce the risk of additional SREs.[12] In light of the slight risk of jaw osteonecrosis associated with OI administration, a pretreatment dental evaluation to assess dentition and potential risk prior to OI use might be necessary. The addition of chemotherapy after EBRT and HT (given sequentially), with or without OI is regarded as less appropriate due to the considerable morbidity of chemotherapy, limited survival benefit, and quality of life during the course of chemotherapy given the lack of visceral tumor burden and the expected symptom control with EBRT, HT, and OI. For this estrogen receptor (ER) positive and progesterone receptor (PR) positive tumor, the use of chemotherapy (with or without OI) and EBRT without HT is deemed inappropriate. Systemic radiopharmaceuticals and surgical intervention are regarded as the least appropriate. For this clinical situation, life expectancy may potentially be measured in years; hence hospice is not typically an appropriate next step.

Table 1. Variant 1

Clinical Condition: Spinal Bone Metastases
A 55-year-old patient with lung cancer with KPS 70 and a history of prior EBRT for a Pancoast tumor, including vertebral levels C7-T4. He received three lines of systemic therapy prior to presenting with symptomatic vertebral metastases (pain scale 6 out of 10) with paraspinous soft-tissue extension from T6–10 with spinal cord compression and mild weakness. Diffuse metastatic disease is noted on bone scan, and multiple small liver metastases are evident on CT of abdomen.

Treatment	*Rating*	*Comments*
Hospice after EBRT	8	
EBRT alone	8	
Direct hospice placement	5	Given the expected poor prognosis, direct hospice placement may be appropriate if pain can be adequately controlled by pharmacologic means.
Chemotherapy and EBRT	3	After progression of disease on third-line therapy there are insufficient data to suggest benefit from additional lines of systemic treatment. Consideration for participation in clinical trials may be given for select individuals.
Chemotherapy and OI and EBRT	2	
Chemotherapy alone	2	
Systemic radiopharmaceuticals	2	
Surgical intervention	2	
Chemotherapy and OI	2	
Radiation therapy dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	3	
40 Gy/20 fractions	2	
Treatment planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical simulation	3	
Posterior field only	7	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior/posterior fields	7	
Posterior obliques	7	
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	1	

Rating Scale: 1,2,3: usually not appropriate; 4,5,6: may be appropriate; 7,8,9: usually appropriate.
CT, computed tomography; EBRT, external beam radiation therapy; ER, estrogen receptor; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; OI, osteoclast inhibitors; PR, progesterone receptor; SBRT, stereotactic body radiation therapy.

HT and OI with analgesics may be considered options for the initial intervention. However, EBRT offers the patient an excellent likelihood of expedient pain control and can be used in conjunction with HT, OI, and analgesics and is a favored approach due to the magnitude of her pain. In this symptomatic spine lesion where disease progression under systemic therapy alone could incur the risk of spinal cord compression, the benefit of adding EBRT to any systemic regimen is emphasized. If EBRT is not administered to the spine at this time, then very close monitoring of the patient would be required to monitor for pain as well as early symptoms of spinal cord compression.

The RT dose fractionation prescribed for spinal metastases varies from those for long bones. Fractionation schedules ranging from a single 8 Gy fraction to 35 Gy in 14 fractions are all considered appropriate, whereas 40 Gy in 20 fractions is considered less appropriate due to the protracted length of therapy. 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 and PA alone, are considered appropriate. Posterior oblique treatment is also an appropriate alternative if the kidneys can be spared, as it is an easy, relatively conformal dosimetric approach that can spare the skin if spinal surgery ever comes into play in the later course of disease. The treating physician will need to judge the risk and benefit of each technique on each individual patient. However, more sophisticated, highly conformal approaches such as SBRT, IMRT, and protons are considered not necessary. Low- to moderate-dose steroids are often used during the course of radiation to vertebral metastases in the absence of spinal cord involvement. (See Table 2.)

Variant 3 Discussion

This patient presents with epidural spinal cord compression at T7 and is without a history of prior therapy for his

Table 2. Variant 2

Clinical Condition: Spinal Bone Metastases
A 55-year-old woman with ER positive/PR positive and HER2 negative breast cancer, and new metastases with symptomatic (pain scale 7 out of 10) vertebral metastases at T12, L1, and L2, with no compression fracture or canal involvement. In addition, she has diffuse asymptomatic metastases on bone scan, rising CEA and no prior EBRT to spine. KPS 80, with no visceral tumor burden. No prior HT.

Treatment	*Rating*	*Comments*
HT and EBRT	8	
HT and OI and EBRT	8	
Chemotherapy and HT and EBRT	5	
Chemotherapy and HT and OI and EBRT	5	
Chemotherapy and EBRT	3	
HT alone	3	
Chemotherapy alone	3	
EBRT alone	3	
Systemic radiopharmaceuticals alone	2	
Surgical intervention	2	
Direct hospice placement	2	
Hospice after EBRT	2	
Radiation therapy dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	5	
40 Gy/20 fractions	3	
Treatment planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical simulation	3	
Posterior field only	7	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior/posterior fields	8	
Posterior obliques	7	This technique helps preserve the skin if surgical intervention of the spine come into play in later course of disease, but it is only deemed appropriate if the kidneys can be spared.
SBRT	3	
IMRT	2	
Proton therapy to the bone metastasis	2	

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate.
CEA, carcinoembryonic antigen; CT, computed tomography; EBRT, external beam radiation therapy; ER, estrogen receptor; HT, hormonal therapy; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; OI, osteoclast inhibitors; PR, progesterone receptor; SBRT, stereotactic body radiation therapy.

multiple myeloma. The main goals of treatment are to decompress the spinal cord and to control the pain. High- to moderate-dose steroid therapy should be started promptly to decrease cord edema/inflammation and act therapeutically against myeloma. Because plasma cell tumors are very radiosensitive even to a low to moderate dose of radiation, the recommended treatment is emergent EBRT.[9] Adding OI to the treatment of multiple myeloma reduces pathologic vertebral fractures, SREs, and pain, and it can be considered in conjunction with EBRT.[23] In light of the slight risk of jaw osteonecrosis associated with OI administration, a pretreatment dental evaluation to assess dentition and potential risk prior to OI use 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. Kyphoplasty procedures may be considered for pathologic vertebral compression fractures but are not indicated in the setting of spinal cord compression.[24] Radiopharmaceuticals are used in multiple myeloma clinical trials, in association with stem cell transplantation.[25] The presence of systemic disease coupled with the patient's reasonably good performance status suggests that systemic treatment should be considered.

Although there are no definitive data to suggest the most appropriate RT dose, fractionation schedules ranging from a single 8 Gy fraction to 40 Gy in 20 fractions are all considered appropriate. Given the fact that the patient is relatively young and has good performance status, the life expectancy can be estimated in years. For this reason, more fractionated regimens, such as 30 Gy in 10 fractions, 35 Gy in 14 fractions, or 40 Gy in 20 fractions, are favored. 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 considered appropriate. A posterior oblique treatment approach is favored, 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 comes into play in the later course of 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. More sophisticated, highly conformal approaches such as SBRT, IMRT, and protons are considered insufficiently studied and therefore unjustified. Furthermore, multiple myeloma is very radiosensitive, rendering radiation dose escalation using advanced technology unnecessary for palliation of pain and spinal cord compression. (See Table 3.)

Variant 4 Discussion

The patient's systemic tumor burden appears stable, and his only symptomatic site is that of the T7 lesion. The case raises the issue of reirradiation of the spine. Reirradiation using EBRT poses an increased risk of radiation myelitis should the patient's lifespan exceed 6 months. Means to treat this symptomatic T7 lesion include surgery, reirradiating, or systemic anticancer interventions with chemotherapy or radiopharmaceuticals. Steroids, OI, and analgesics may improve pain control and should be used. Surgery may be considered if the adjacent, irradiated bone appears stable and the patient's life expectancy is >3–6 months. The decision to proceed with surgery in this situation is very nuanced; patients with vertebral body compression fracture alone without significant mechanical instability are often helped with

Table 3. Variant 3

Clinical Condition: Spinal Bone Metastases
A 54-year-old man presents with newly diagnosed multiple myeloma. He develops mild bilateral lower-extremity weakness (motor power 5 minus out of 5) from an epidural spinal cord compression at T7 seen on MRI, associated with severe pain (scale 8 of 10). KPS 80. Skeletal survey reveals several other sites of asymptomatic lytic metastases.

Treatment	*Rating*	*Comments*
Steroid therapy and EBRT, followed by OI and chemotherapy	8	EBRT sequentially with systemic therapy.
Steroid therapy and EBRT, followed by chemotherapy	7	
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	3	
Steroid therapy alone	2	
OI alone	2	
Hospice after EBRT	2	Life expectancy would be expected to be >6 months.
Observation	1	
Systemic radiopharmaceuticals alone	1	
Direct hospice placement	1	Life expectancy without treatment still could be >6 months, although paraplegia would be expected to occur.
Radiation therapy dose		
8 Gy/1 fraction	6	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	6	
40 Gy/20 fractions	5	
Treatment planning		
CT simulation	8	
Fluoroscopic simulation	8	
Clinical simulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior/posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in later course disease but it will result in higher lung doses.
SBRT	2	
IMRT	2	
Proton therapy to the bone metastasis	1	

Rating Scale: 1,2,3: usually not appropriate; 4,5,6: may be appropriate; 7,8,9: usually appropriate.
CT, computed tomography; EBRT, external beam radiation therapy; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; MRI, magnetic resonance imaging; OI, osteoclast inhibitors; SBRT, stereotactic body radiation therapy.

Table 4. Variant 4

Clinical Condition: Spinal Bone Metastases
A 72-year-old man with non-small-cell lung cancer, 2 years status post right upper lobectomy with a KPS of 80. He received previous RT to the T5-T8 spine 10 months ago to 30 Gy in 10 fractions. He also received two lines of systemic chemotherapy. Now he presents with debilitating pain (pain scale 8 out of 10) from recurrent disease at T7 with no canal involvement. Diffuse asymptomatic bone metastasis, stable on bone scan with no visceral metastases.

Treatment	*Rating*	*Comments*
Surgical intervention alone	6	Surgery may be considered if the adjacent, irradiated bone appeared stable and the patient's life expectancy was >3–6 months.
EBRT alone	6	EBRT in the form of SBRT or IMRT if they are available and sustained positioning is achievable for the patient.
Surgical intervention and EBRT	6	If life expectancy >3–6 months; EBRT in the form of SBRT if they are available and sustained positioning is achievable for the patient. See comments about surgery in text.
Surgical intervention and EBRT and systemic radiopharmaceuticals	5	If life expectancy >3–6 months; EBRT in the form of SBRT if they are available and sustained positioning is achievable for the patient.
Surgical intervention and systemic radiopharmaceuticals	5	
Hospice after treatment (surgery or SBRT) of the spine	5	
Systemic radiopharmaceuticals alone	3	
Direct hospice placement	3	
Chemotherapy	4	Third-line chemotherapy with erlotinib may be considered for individuals who have a good performance status and who have not had prior exposure to erlotinib or gefitinib. There are insufficient data addressing use of additional cytotoxic drugs; considerations may be given to clinical trials and best supportive care.
OI alone	3	
SBRT dose		
12–18 Gy/1 fraction	7	Spinal cord tolerance permitting.
21–27 Gy/3 fractions	7	Spinal cord tolerance permitting.
20–30 Gy/5 fractions	7	Spinal cord tolerance permitting.
Treatment planning		
CT simulation	9	CT simulation is mandatory if SBRT is offered because sophisticated dose planning is required.
Fluoroscopic simulation	3	
Clinical simulation	3	
Posterior field only	3	
Anterior/posterior fields	3	
Posterior obliques	3	
SBRT	7	Treatment planning technique depends on treatment device used.
IMRT	6	
Proton therapy to the bone metastasis	2	

Rating Scale: 1,2,3: usually not appropriate; 4,5,6: may be appropriate; 7,8,9: usually appropriate.
CT, computed tomography; EBRT, external beam radiation therapy; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; OI, osteoclast inhibitors; SBRT, stereotactic body radiation therapy.

vertebral augmentation procedures such as kyphoplasty or vertebroplasty.[26] 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. There is little information to provide guidance on reirradiation of spinal metastases. Goals of treatment include obtaining pain relief while minimizing the risk of radiation myelitis. Highly conformal techniques such as proton therapy, SBRT, or IMRT can be considered if they are available and if sustained positioning is achievable for the patient. Ideally, the patient can enroll 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 deemed appropriate provided the cord tolerance can be respected.[27] Surgery can provide rapid relief of debilitating pain and may be considered given the patient's good performance status. Because there is no spinal canal involvement in this case, systemic

Table 5. Variant 5

Clinical Condition: Spinal Bone Metastases
A 56-year-old postmenopausal woman with ER positive/PR positive and HER2 negative breast cancer and a KPS of 90. At diagnosis, she developed a painful, solitary, biopsy-proven bone metastasis at T4 level with no canal involvement or compression fracture/spinal instability and no other sites of metastasis.

Treatment	*Rating*	*Comments*
HT and EBRT	8	
HT and OI and EBRT	8	
Chemotherapy and HT and EBRT	5	
Chemotherapy and HT and OI and EBRT	5	
HT and OI	4	
HT alone	4	
Chemotherapy alone	3	
Surgical intervention	3	
Systemic radiopharmaceuticals alone	2	
OI alone	2	
Direct hospice placement	1	Life expectancy would be expected to be >6 months.
Hospice after EBRT	1	Life expectancy would be expected to be >6 months.
Radiation therapy dose		
8 Gy/1 fraction	8	
20 Gy/5 fractions	8	
30 Gy/10 fractions	8	
35 Gy/14 fractions	5	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data are needed to better define the role of this approach.
40 Gy/20 fractions	5	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data are needed to better define the role of this approach.
Treatment planning		
CT simulation	8	CT simulation is mandatory if SBRT is offered because sophisticated dose planning is required.
Fluoroscopic simulation	8	
Clinical simulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used. The skin dose is a concern for this patient who is expected to have more favorable prognosis as spinal surgery may be needed in the later course of her disease.
Anterior/posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in the later course of disease but it will result in higher lung doses.
SBRT	No consensus	There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data are needed to better define the role of SBRT in this type of clinical scenario.
IMRT	2	
Proton therapy to the bone metastasis	1	

Rating Scale: 1,2,3: usually not appropriate; 4,5,6: may be appropriate; 7,8,9: usually appropriate.
CT, computed tomography; EBRT, external beam radiation therapy; ER, estrogen receptor; HT, hormonal therapy; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; OI, osteoclast inhibitors; PR, progesterone receptor; SBRT, stereotactic body radiation therapy.

therapies, including radiopharmaceuticals, could be given either as an adjuvant or alone if surgery is not a practical approach. Third-line chemotherapy with erlotinib may be considered for individuals who have a good performance status and who have not had prior exposure to erlotinib or gefitinib. There are insufficient data addressing use of additional cytotoxic drugs; considerations may be given to clinical trials and best supportive care.[19] (See Table 4.)

Variant 5 Discussion

This patient has a good performance status, a relatively long life expectancy, and a solitary site of painful metastasis in a vertebra without canal involvement. This clinical scenario qualifies as a case of oligometastasis.[28] The optimal management of oligometastases is an active area of research. Investigations of site-specific localized therapy

Table 6. Variant 6

Clinical Condition: Spinal Bone Metastases
A 45-year-old woman with metastatic renal cell carcinoma, involving her lungs and T9, and a KPS of 90, received sunitinib and developed progressive single spinal metastasis at T9 with no canal involvement or compression fracture. Her other extraspinal metastases in the lungs and right adrenal were stable.

Treatment	*Rating*	*Comments*
Systemic therapy and EBRT	7	
Systemic therapy and EBRT and OI	7	
Systemic therapy and OI	5	
Systemic therapy alone	4	
EBRT alone	3	
Surgical intervention	3	
OI alone	3	
Systemic radiopharmaceuticals alone	2	
Direct hospice placement	2	
Hospice after EBRT	2	
Radiation therapy dose		
8 Gy/1 fraction	5	
20 Gy/5 fractions	7	
30 Gy/10 fractions	7	
35 Gy/14 fractions	7	
40 Gy/20 fractions	5	
20–30 Gy/5 fractions (SBRT)	7	Spinal cord tolerance permitting.
18–27 Gy/3 fractions (SBRT)	7	Spinal cord tolerance permitting.
15–24 Gy/1 fraction (SBRT)	7	Spinal cord tolerance permitting.
Treatment planning		
CT simulation	9	CT simulation is mandatory if SBRT is offered because sophisticated dose planning is required.
Fluoroscopic simulation	7	
Clinical simulation	5	
Posterior field only	6	The depth of the spinal segments involved and photon energy used are to be considered if this technique is used.
Anterior/posterior fields	7	
Posterior obliques	7	This technique can help preserve skin if spinal surgery comes into play in the later course of disease but it will result in higher lung doses.
SBRT	7	Because renal cell carcinoma is radioresistant histology, there may be a benefit to using SBRT, which delivers ablative doses of radiation to the spinal metastatic lesion.
IMRT	4	
Proton therapy to the bone metastasis	1	

Rating Scale: 1,2,3: usually not appropriate; 4,5,6: may be appropriate; 7,8,9: usually appropriate.
CT, computed tomography; EBRT, external beam radiation therapy; IMRT, intensity-modulated radiation therapy; KPS, Karnofsky performance status; OI, osteoclast inhibitors; SBRT, stereotactic body radiation therapy.

compared with a more systemic approach with or without localized therapy are ongoing. Some have argued that patients with minimal sites of bone-only metastatic disease (deemed "oligometastatic") may be treated with curative intent, although the data to confirm that stance are still limited. The use of HT and OI, with or without sequential EBRT, is regarded as one of the reasonable treatment options. For this ER positive/PR positive tumor, where there is no visceral involvement, a localized therapy may be considered, ideally as part of a clinical trial. Systemic therapy is typically administered due to the likelihood of systemic involvement.[29] Surgical intervention is regarded as less appropriate given the absence of spinal cord compression or spinal instability and alternative methods of providing site-specific disease control. Systemic radiopharmaceuticals are regarded as the least appropriate and have not been formally studied in the setting of newly diagnosed oligometastatic disease.

If EBRT is not administered to the spine at this time, then very close monitoring of the patient would be required to monitor for pain, and for early symptoms of spinal cord compression. Because this patient's survival is likely to be measured in years, hospice placement is deemed an inappropriate option.

The RT dose fractionation prescribed varies from those for long bones. Fractionation schedules ranging from a single 8 Gy fraction to 40 Gy in 20 fractions are all considered appropriate.[30–33] 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 and PA alone, are considered

appropriate. Posterior oblique treatment is favored as it is an easy, relatively conformal dosimetric approach that can reduce the skin dose, and this may be beneficial if spinal surgery comes into play in the later course of 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. In this setting of spinal oligometastasis and the absence of extraspinal metastasis, if aggressive local therapy is part of the treatment regimen, SBRT or IMRT aimed at delivering a higher biologically effective dose to improve local control may be considered appropriate, particularly as part of a clinical trial.[6,8] The relatively limited availability and much higher cost render proton beam therapy not appropriate. (See Table 5.)

Variant 6 Discussion

This patient has a good performance status and a single site of painful and progressive metastasis in a vertebra without canal involvement. Standard analgesics should be used for initial pain control. Renal cell carcinoma is regarded as a radioresistant histology and may not be as responsive to EBRT in the palliative dose range, although some palliative response has been observed.[34,35] The use of EBRT with sequential systemic therapy with or without OI is deemed appropriate. Surgical intervention is not routinely offered in the absence of spinal cord compression or spinal instability. Systemic radiopharmaceuticals are regarded as the least appropriate.

Especially in this symptomatic spine lesion where disease progression under systemic therapy alone could incur the risk of spinal cord compression, the benefit of adding EBRT to systemic therapy in a sequential fashion is again emphasized. If EBRT is not administered to the spine, then very close monitoring of the patient would be required to assess for pain, and for early symptoms of spinal cord compression.

Given the radioresistant nature of renal cell carcinoma, a more aggressive dose regimen is deemed appropriate.[34,36] If SBRT is available, it is best used in a clinical trial setting. SBRT regimens using 1–5 fractions are deemed appropriate. This should be combined with systemic therapy sequentially because the systemic disease still needs to be addressed. Fractionation schedules delivering a higher dose, such as 30 Gy in 10 fractions, 35 Gy in 14 fractions, or 40 Gy in 20 fractions, are deemed appropriate.[30–33] SBRT dose regimens include 16–24 Gy in 1 fraction, 24–27 Gy in 3 fractions, and 30 Gy in 5 fractions, and they are all regarded as appropriate provided that spinal cord tolerance is respected.[37] CT simulation is required to accurately include the involved vertebrae and account for body habitus in SBRT dose calculation. CT simulation is also desirable if EBRT is used. Fluoroscopic simulation is regarded as a reasonable alternative. Common EBRT field arrangements, AP/PA and PA alone, are considered appropriate. A posterior oblique treatment approach is most favored as it is an easy, relatively conformal, dosimetric approach that can reduce the volume of the RT dose administered to the esophagus within the EBRT field. The relatively limited availability renders proton beam therapy not practical. (See Table 6.)

Summary

- EBRT successfully provides rapid palliative relief from painful spinal bone metastases in the majority of cases.
- The acute side effects of palliative EBRT are usually minimal and self-limiting, whereas long-term side effects are uncommon and often irrelevant in a patient group with limited life expectancy.
- In good performance status patients with epidural spinal cord compression, surgical decompression should be considered, and this should be followed by EBRT if no EBRT has been given before in the same area.
- Prospective randomized trials have proven that equivalent pain relief can be achieved with varied fractionation schemes including a single 8 Gy, 20 Gy in 5 fractions, 24 Gy in 6 fractions, or 30 Gy in 10 fractions. Prolonged courses are associated with a lower incidence of retreatment, whereas shorter courses maximize patient and caregiver convenience.
- Reirradiation of spinal metastasis may be achieved using highly conformal techniques such as SBRT, IMRT, and proton beam therapy, although retreatment can carry a higher risk of radiation myelitis. Ideally, if there is a clinical trial available, patients should be enrolled to be treated on protocol. Surgical intervention should be considered in patients with previously irradiated spinal metastases causing severe pain or spinal compression.
- Highly conformal techniques such as SBRT, IMRT, and proton beam therapy for spinal cord compression are best tested in a clinical trial setting.
- There may be a potential survival benefit to aggressive local therapy of oligometastasis but more data are needed to better define the role of highly conformal RT techniques that allow for radiation dose escalation in this type of clinical scenario.
- Other treatments such as analgesics, including narcotic analgesics and steroids, should be used initially for pain control in most cases.
- OI can be incorporated into palliative care of skeletal complications from spinal metastasis.
- Management of metastatic bone disease is palliative. A multidisciplinary team of care providers should be available to the patient, including the palliative care team. Goals of care should be defined with the patient. Hospice referral should be considered if the patient's life expectancy is $\leq$6 months.

For additional information on ACR Appropriateness Criteria®, refer to the ACR website (www.acr.org/ac).

Acknowledgments

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Author Disclosure Statement

No competing financial interests exist.

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