Radiation for Spinal Metastatic Tumors

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• Stereotactic • Radiosurgery • SBRT • SRS
• Spinal • Vertebral • Radiotherapy

IRRADIATION FOR SPINAL METASTATIC TUMORS

In autopsy studies, metastases are found in the vertebral bodies of 5% to 30% patients who have malignant disease.[1–4] At autopsy, vertebral metastases have been found in as many as 90% of patients who had prostate cancer 74% of patients who had breast cancer, 45 % of patients who had lung cancer, 29% of patients who had lymphoma, and 25% of patients who had gastrointestinal malignancies.[5] Up to 20% of these spinal metastases are symptomatic, with associated severe pain, limitation of motion, increasing requirements for pain medication, decreasing quality of life, and potentially decreased duration of life secondary to complications arising from symptoms. Epidural spinal cord compression ultimately occurs in 5% to 15% of patients who have cancer, further degrading the overall quality of life and shortening the duration of life.[1–3,6,7] Pain is present in 83% to 95% of these cases, and two thirds of patients who have cord compression are nonambulatory at presentation.[5,8] Sensory deficits are associated with the compression in 40% to 90% of patients.[5]

Standard methods for dealing with these symptomatic occurrences include the delivery of radiation (alone or in conjunction with chemotherapy), radionuclide therapy, hormonal therapy, bisphosphonate therapy, and surgical decompression (with or without adjunctive irradiation). The magnitude of the problem is increasing as patients with more common malignancies (breast, prostate and lung cancer) survive for longer lengths of time because of the development of new and more effective treatment strategies. The need to prevent or manage the complications arising from spinal involvement is becoming a greater challenge to the clinician, because the short-term duration of control of areas of vertebral involvement is inadequate. At the same time, longer survival posttherapy allows more time for complications resulting from overly aggressive approaches to become manifest. New approaches involving the delivery of much larger doses of radiation in single fraction (stereotactic radiosurgery, SRS), hypofractionated regimens (stereotactic body radiotherapy, SRT or SBRT), or the use of particle therapy (protons) are showing increasing efficacy and duration of control in long-term survivors.

The selection of an appropriate therapeutic intervention depends on a number of factors: histology, extent of disease, existing comorbidities, age of the patient, prior treatment modalities, predicted life expectancy, and availability of resources. Some form of irradiation usually is recommended when the vertebral lesions cause significant pain[9] or neurologic symptoms resulting from nerve root or cord compression[5] or, increasingly, in patients who have oligometastases and a diagnosis with a prolonged life expectancy, such as prostate or breast cancer.[10–16]

Standard External Beam Therapy

For patients who have widely metastatic disease and a relatively short life expectancy, palliation of symptoms is the main reason for considering radiation therapy for spinal metastases. The timing and delivery of the radiation must take into account the past use of and future plans for systemic therapies, because the combined administration of extensive fields of large-dose-per-fraction radiation and certain types of chemotherapies and biologic modifiers may increase the risk of severe toxicity to an already debilitated patient.

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Not all sites of vertebral involvement require radiation intervention. Sites that are actively causing pain, sites of vertebral collapse, and certainly sites with neurologic consequences resulting from spinal cord, cauda, or nerve root compression should be addressed in a timely fashion. It often is difficult to decide exactly how much of the spine to treat in patients who have diffuse involvement of the spinal column demonstrated on bone scans or MRI. Areas that are small and asymptomatic, unless immediately adjacent to the more significant sites that require treatment, may be spared to minimize the impact on marrow capacity for future systemic therapies. These asymptomatic sites should be addressed with the use of bisphosphonates,[17–21] with chemotherapy, or with future irradiation should they become symptomatic.

A prospective, randomized study of 123 patients who had new-onset cord compression (ie, major symptoms present for <48 hours) found initial surgical decompression followed by postoperative irradiation to be superior to irradiation alone in terms of ambulatory rates, maintenance of continence, motor strength, and reduction in long-term opioid and steroid requirements.[6] Patients who had a life expectancy of more than 3 months, duration of paraplegia for less than 48 hours, a single area of radiologically documented spinal cord displacement, and no prior history of spinal cord compression were assigned randomly to either immediate surgical decompression followed within 14 days by irradiation or to irradiation alone to a dose of 30 Gy. Patients who had very radiosensitive tumors (lymphomas, myelomas, germ cell tumors), and those who had brain metastases were excluded from the study. The posttreatment ambulatory rates were 84% for surgery versus 57% for irradiation alone ($P < .001$). The median length of time that patients maintained the ability to walk was 122 days after surgical decompression versus only 13 days after irradiation alone. Of the patients who were able to walk at entry into the study, 94% of those treated with the combined approach continued to be ambulatory, compared with 74% of those treated with irradiation alone. Of those unable to walk at entry into the study, 62% in the surgical decompression group regained the ability after surgery, versus 19% in the irradiation group. These results clearly show a benefit of immediate surgical decompression followed by irradiation in those patients who met the eligibility criteria.

Not all patients who have cord compression necessarily require surgical intervention, however. Based on a multivariate analysis performed on a cohort of 2096 patients who were irradiated for spinal cord compression without surgery from 1992 to 2007, Rades and colleagues[1] proposed a scoring system with the potential to predict the ambulatory rates after irradiation alone using five prognostic factors: histology, the interval between initial diagnosis of malignancy and development of cord compression (<15 months or >15 months), the presence of visceral metastases, pretreatment motor function (ambulatory versus nonambulatory), and the duration of motor deficits before irradiation (1–7 days, 8–14 days, or >14 days). As in Patchell's study, this scoring system identified a subset of patients who had excellent postradiotherapy ambulatory rates who might not require surgical decompression. These patients met all the following criteria: favorable histology (myeloma/lymphoma, breast, prostate), more than 15 months between diagnosis and the development of cord compression, ambulatory before radiotherapy, and slower development of motor deficits (>14 days). Postradiotherapy ambulatory rates of 99% were seen in 750 of 760 patients who met these criteria and underwent irradiation alone.

Irradiation without surgery often is appropriate for patients without evidence of structural instability or epidural cord compression, especially for patients who have radiosensitive histologies (lymphoma, myeloma, germ cell tumors, prostate cancer, or breast cancer). The area treated traditionally has been the involved vertebra(e) plus one additional body above and below the target area. Bone scans or MRIs are helpful in defining the field sizes. The radiation beam delivery approach is determined by the level of the spine involved, the presence nearby of radiosensitive organs such as the kidneys, upper esophagus, and lungs, and any areas of prior irradiation that might overlap with the current area. Simple opposed anterior and posterior fields often are the best choice for the minimizing radiation exposure of nearby organs in thoracolumbar and sacral lesions. Posterior wedge pairs for lumbar lesions may reduce the bowel toxicity (diarrhea, nausea) while respecting the radiation tolerance of the kidneys and liver. Special care is taken with cervical lesions to minimize the risk of severe esophageal irritation; opposed lateral fields are used to minimize esophageal exposure. This precaution is especially important in patients being treated with concurrent systemic therapy, such as taxanes, that may increase the risk of radiation esophagitis dramatically.

The dose fractionation schedule used in these palliative cases has been the focus of a large number of prospective, randomized trials. A recent meta-analysis of 16 major trials worldwide comparing multiple fractionation schemes for palliation of pain secondary to bone metastases failed to

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