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REVIEW ARTICLE

The current status and future of radiotherapy for spinal bone metastases

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Abstract The management of spinal bone metastases is complex. In this review, the efficacy, methodology, and utilization of radiotherapy (RT) for spinal bone metastases are discussed. A number of randomized trials have evaluated the efficacy of 8 Gy, single-fraction RT for the palliation of painful bone metastases. However, RT for metastatic spinal cord compression has not been evaluated with respect to its optimal dose, palliative potential, or its ability to improve motor function. Two highly sophisticated RT techniques — stereotactic body RT (SBRT) and intensity-modulated RT (IMRT) — have recently been adapted for the treatment of spinal bone metastases, and both have the potential to achieve excellent control while minimizing acute and late toxicity. SBRT and IMRT are particularly well suited for the treatment of spinal bone metastases when they are localized or require re-irradiation, and may provide superior tumor control. Predicting the prognosis of patients with bone metastases and assessing spinal instability are both important when selecting the optimal RT method and deciding whether to perform surgery. The proper care of spinal bone metastases patients requires an interdisciplinary treatment approach.

Introduction

Bone metastases are a common manifestation of malignancy that can cause severe and debilitating effects, including pain, spinal cord compression, hypercalcemia, and pathologic fractures. The proper care of patients with bone metastasis requires interdisciplinary treatment delivered by orthopedic surgeons, radiation oncologists, medical oncologists, pain medicine specialists, radiologists, and palliative care professionals. Radiotherapy (RT) can provide successful palliation of painful bone metastasis in 50–80 % of patients in a time efficient manner, and is associated with very few adverse effects, allowing complete pain relief at the treated site in up to one-third of patients [1]. Recently, in the field of radiation oncology, emerging novel techniques have been developed and adapted for the treatment of bone metastases. In light of these advances, the focus of this review includes the efficacy of RT, new RT methods, and relevant prognostic factors. The significance of each of these in the management of spinal bone metastases is discussed.

Radiation dose and schedule

RT is commonly used to provide pain relief in cases of painful bone metastases. Chow et al. [2] conducted a meta-analysis of 25 randomized palliative RT trials for uncomplicated painful bone metastases comparing 8 Gy in single and 20–30 Gy in multiple fractions. They concluded that both the overall pain relief rate (60 % in the single-fraction arm and 61 % in the multiple-fraction arm) and the complete pain relief rate (23 and 24 %, respectively) were similar with no significant difference between these schedules. Although retreatment rates were higher in those who received single-fraction therapy, 8 Gy in single-fraction RT was suggested as the standard of care for the palliation of uncomplicated painful bone metastases in the recent American Society for Therapeutic Radiology and Oncology guidelines [3].

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It is possible that patients with metastatic spinal cord compression (MSCC) will benefit more from higher-dose multiple-fraction RT than they would from lower-dose single-fraction RT, although currently, there is little data to support this (Table 1). In their review, Chow et al. [1] found that spinal cord compression occurred in 5.7 and 4.1 % of patients who received single-fraction and multiple-fraction RT, respectively. Although there was a trend favoring multiple-fraction RT, this did not reach statistical significance ($P = 0.31$). Rades et al. [4] evaluated the local control achieved using different RT schedules for MSCC. In their prospective, non-randomized study, local control was found to be significantly better after a long course of treatment (30 Gy in 10 fractions, 37.5 Gy in 15 fractions, and 40 Gy in 20 fractions) compared to a shorter course (8 Gy in a single-fraction, and 20 Gy in 4 fractions). In contrast, Maranzano et al. [5] demonstrated that a single-fraction RT was sufficient, and resulted in only minimal toxicity for patients with a poor prognosis.

Rades et al. [6] suggested in their retrospective study that dose escalation beyond 30 Gy in 10 fractions did not improve motor function and local control of MSCC in radioresistant tumors, such as renal cell carcinoma, colorectal cancer, and malignant melanoma. However, in another report [7], dose escalation beyond 30 Gy was found to give better local control and extend overall survival in patients with breast cancer, prostate cancer, myeloma/lymphoma, and others who had a favorable prognosis. Thus, 30 Gy in 10 fractions could be regarded as the standard therapeutic dose for MSCC. Although the available evidence is limited, dose escalation beyond 30 Gy may improve local control and overall survival in patients with a favorable survival prognosis, but it may not improve functional outcome, and dose escalation to 40 Gy in 20 fractions may still be insufficient for radioresistant tumors.

IMRT and stereotactic body RT

Recently, two sophisticated RT techniques, stereotactic body RT (SBRT; including stereotactic radiosurgery and stereotactic RT) and intensity-modulated RT (IMRT) have been adapted for the treatment of spinal bone metastases. SBRT uses more beams from many more directions than conventional opposed-field RT and consequently delivers much higher doses in a hypofractionated manner (either as a single fraction or as a smaller number of fractions). IMRT makes it possible to deliver optimal radiation doses safely to an irregularly shaped target while minimizing the dose to the surrounding normal structures. In order to achieve a high standard of targeting precision, these approaches require that the exact location and shape of the tumor be determined using imaging techniques (Fig. 1). In general, the term "spinal SBRT" refers to the use of both IMRT techniques and SBRT. The most important additional benefit of spinal SBRT is the possibility of achieving excellent dose coverage of the target, while avoiding the spinal cord, which is often the major limiting factor when delivering high-dose RT (Figs. 1, 2). Multiple retrospective studies have demonstrated that SBRT could feasibly be used to treat spinal metastases, and could control target lesions with only low toxicity [8, 9]. The local control rate based on imaging and/or pain management criteria was reported to be greater than 80 %, with only rare cases of toxicity.

Table 1 Outcomes of conventional RT for MSCC

References	Study design	State of disease	Dose	Ambulatory rate before treatment (%)	Motor function improvement (%)	LC	Overall survival
Maranzano [5]	RCT	Unfavorable prognosis	8 Gy/1 Fr	64	12	NA	4 months (median)
			16 Gy/2 Fr	67	21	NA	4 months (median)
Rades [4]	Prospective non-RCT	Various	8 Gy/1 Fr, 20 Gy/4 Fr	61	37	61 % at 1 years	23 % at 1 year
			30–40 Gy/10–20 Fr	62	39	81 % at 1 years	30 % at 1 year
Rades [7]	Matched cohort	Favorable prognosis	30 Gy/10 Fr	85	40	71 % at 2 years	53 % at 2 years
			37.5 Gy/15 Fr 40 Gy/20 Fr	85	41	92 % at 2 years	68 % at 2 years
Rades [6]	Retrospective	Radio-resistant tumor	30 Gy/10 Fr	62	18	76 % at 1 year	NA
			37.5 Gy/15 Fr 40 Gy/20 Fr	63	22	80 % at 1 year	NA

RT radiotherapy, *MSCC* metastatic spinal cord compression, *LC* local control, *RCT* randomized controlled trial, *Fr* fraction, *NA* not available