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Overview

Re-irradiation of Vertebral Body Metastases: Treatment in the Radiosurgery Era

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Abstract

Vertebral bodies remain one of the most common sites of metastases. In cases where surgical intervention is not indicated or appropriate, conventional external radiation therapy (cEBRT) has been the standard treatment modality. Unfortunately, cEBRT is typically limited, with low complete response and poor local control rates. Disappointing results with re-irradiation using cEBRT highlight the need for innovative salvage therapeutic strategies, such as stereotactic body radiotherapy. A detailed description of this complex treatment strategy is outlined, as is a systematic review of current literature. Although data are limited to single institution series, re-irradiation has consistently been found to be effective with respect to local control (1 year rates range from 66 to 90%) and pain response. Importantly, the treatment is shown to be safe, with the crude rate of radiation myelopathy <1% and a rate of vertebral compression fracture of 12%. As further research and technologic advances continue to refine therapy, stereotactic body radiotherapy is now a recommended option for the treatment of previously irradiated vertebral body metastases.

Key words: Metastases; re-irradiation; spine; vertebral body

Statement of Search Strategies Used and Sources of Information

The intent of this review is to address the role of re-irradiation in the management of vertebral body metastases. A systematic literature search was carried out using MEDLINE, PubMed and Embase databases, with the last search date July 2017. Subject headings included: 'spine', 'vertebral bodies', 'radiotherapy', 'radiation', 'stereotactic radiosurgery', 'stereotactic body radiotherapy', 'SRS' and 'SBRT'.

Introduction

Vertebral bodies remain one of the most common sites of metastases, with incidence rates approaching 40% [1]. These metastases can cause significant morbidities, including pain, mechanical instability, radiculopathy and catastrophic neurological dysfunction related to malignant epidural spinal cord compression. In cases where surgical intervention is not indicated or appropriate, conventional external radiation therapy (cEBRT) has been the standard treatment modality [2]. Unfortunately, cEBRT is typically limited, with complete responses rates to pain of less than 20% and poor local control rates, especially for bulky spinal metastases [3,4].

The traditional intent of cEBRT has been strictly palliative, with various low dose cEBRT utilised to balance toxicity and patient convenience with efficacy in patients felt to have limited prognosis. Several large international trials randomising patients to various low dose cEBRT schemes have consistently reported that within the first 3–6 months about 20% of patients will need retreatment for failed treatment efficacy. This may be more of an issue in modern oncological care, given novel compounds able to extend patient survival well beyond a year despite having even extensive metastatic disease.

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The salvage of cEBRT failures has traditionally been a second course of cEBRT, with an even lower biologically equivalent dose (BED) than first delivered. This principle is based on respecting the cumulative radiation tolerances of the normal tissues and a function of the lack of conformity in the dose distribution given that the entire volume is radiated homogeneously. Uncontrolled retrospective series have suggested a modest benefit to re-irradiation [5] and often patients are left for hospice or medical management. In 2014, the SC.20 phase III randomised controlled trial was reported, representing an international effort led by the Canadian Clinical Trials Group. This study randomised patients with previous conventionally radiated painful bone metastases (28% of patients had vertebral body metastases) to 8 Gy/one fraction or 20 Gy/five fractions or 20 Gy/eight fractions [6]. An intention to treat analysis revealed disappointing results, with an overall pain response of around 30% and a complete pain response of 8%. Therefore, although there is a suggestion of efficacy, the trial highlights the need for innovative therapeutic strategies to improve outcomes.

One such innovation has been the development of stereotactic body radiotherapy (SBRT), which is defined as the precise delivery of highly conformal, image-guided and hypofractionated EBRT [7]. The fundamental principles of this technique for the spine have been previously described, but in brief include complex simulation and target definition, rigid immobilisation, high dose per fraction and rigorous image-guided treatment delivery [7]. Ultimately, spine SBRT needs to deliver with an overall precision of less than 2 mm [8]. Spine SBRT allows for tumour dose escalation while differentially dosing the spinal cord to a lower and tolerant dose; this is most relevant in the re-irradiation setting given the compromise needed in spinal cord exposure. In fact, the first application of spine SBRT was for re-irradiation of spinal metastases. Since that original report by Hamilton *et al.* [9], spine SBRT is increasingly practiced. With at least a decade of experience and several published series specific to re-irradiation a great deal has been learned with respect to optimising the technique, dose tolerances and outcomes. This review summarises the state of the art specific to spine SBRT in the re-irradiation scenario, and the approach from the Odette Cancer Centre, Sunnybrook Health Sciences Center, University of Toronto.

Technical Requirements for Spine Stereotactic Body Radiotherapy

The technique at the Odette Cancer Centre is based on the patient immobilised in the BodyFIX near-rigid body device (Elekta AB, Stockholm, Sweden) due to reported reduced planning target volume [10] as compared with less robust immobilisation methods. For cervical and upper thoracic tumours (T3 vertebrae and above), a five-point reinforced thermoplastic mask is the immobilisation strategy of choice. With respect to patient position correction on the treatment table, once the cone-beam computed tomography is acquired, a 6 degree-of-freedom robotic couch is used for correction of fine translations and rotational shifts. Together with near-rigid body immobilisation, patient position reproducibility is reported to be within 1.2 mm and 0.9 degrees with 95% confidence [8].

Simulation requires a 1 mm thin slice computed tomography and fusion with volumetric thin-slice axial T1 and T2 magnetic resonance images (MRI) encompassing at least one vertebral body above and below the target spinal segment(s). Of note, the 1.5 T Phillips MRI simulator has improved fusions due to the flat table top and the ability to image in a five-point head and shoulder mask for cervical–upper thoracic vertebral body metastases. In those infrequent scenarios where the fusion may be unreliable typically due to scoliosis or the imaging artefacts/distortions are significant due to implanted hardware, patients will have a treatment planning computed tomography myelogram. Target and organ-at-risk delineation is based on the MRI; typically, the T1 sequence is the sequence of choice as both the spinal cord and tumour within the bone is visualised on the T1. The T2 image can help with spinal cord delineation and delineation of paraspinal/epidural disease where the T1 image is not sufficient. However, both computed tomography and MRI are essential for volume delineation as computed tomography provides the information with respect to disease within the bone itself and characterisation of lytic versus blastic versus mixed. The clinical target volume delineation approach is based on published guidelines from the International Spine Research Consortium [11]. However, a 5 mm margin beyond any paraspinal soft tissue disease and 5 mm beyond epidural disease both within the axial plane and in the craniocaudal direction is applied. This clinical target volume approach is utilised in the SC.24 Canadian Clinical Trials Group Randomized Trial comparing 20 Gy in five fractions of conventional radiation with 24 Gy in two SBRT fractions. We apply a 2 mm planning target volume, a 1.5 mm planning organ-at-risk volume (PRV) on the true cord; for the cauda equina we contour the thecal sac with no applied PRV.

Figure 1 outlines the inherent dosimetric differences between cEBRT and spine SBRT. Figure 1A and 1B show MRI at initial presentation of a T12 painful spinal metastasis from breast cancer treated with cEBRT (20 Gy in five fractions). Figure 1C is the cEBRT plan where a four-field technique was used and shows the significant amount of normal tissue irradiated and the homogeneous dose distribution that encompasses both target volume and spinal cord. The lesion ultimately progressed within the epidural space and bone. The vertebrae also fractured requiring a cement augmentation procedure and biopsy that confirmed viable tumour (Figure 1D, E). As a result, the patient was subsequently salvaged with SBRT delivering 24 Gy in two fractions and a cord PRV of 12.2 Gy. The dose distribution is distinctly different than the cEBRT plan with the conformal nature of the dose within the vertebral body, sparing of the surrounding normal tissues and a steep dose gradient at the spinal cord interface.

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