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Original Article

Stereotactic Ablative Body Radiotherapy for the Treatment of Spinal Oligometastases

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Abstract

Aims: To report multicentre outcomes of patients with spinal oligometastases treated with stereotactic ablative body radiotherapy (SABR). The primary objective was to estimate the widespread failure-free survival (WFFS) at 2 years – defined as freedom from metastases not amenable to local salvage therapy and death.

Materials and methods: Patients with one to three metastases treated with spinal SABR between January 2010 and July 2014 at four academic institutions were included in this retrospective review. The median dose/fractionation was 24 Gy (range 16–52.5 Gy) in two fractions (range one to three) and the median biologically effective dose ($\alpha/\beta = 10$) was 52.5 Gy (range 40–144.4 Gy). The WFFS, overall survival, freedom from local progression and toxicity rates were described using Kaplan–Meier statistics.

Results: In total, 60 patients with 72 spinal metastases were analysed. The median follow-up was 21 months. Patients had a median age of 66 years, Eastern Cooperative Oncology Group performance 0–1 in 97% and metachronous oligometastases in 85%. The 1 and 2 year WFFS rates were 67% (95% confidence interval 55–80) and 59% (95% confidence interval 47–75), respectively. The 1 and 2 year overall survival rates were 90% (95% confidence interval 83–98) and 76% (95% confidence interval 64–91), respectively. The 1 and 2 year freedom from local progression were 92% (95% confidence interval 85–99) and 86% (95% confidence interval 75–99), respectively. There were four cases (6.7%) of vertebral compression fracture and no cases of radiation myelopathy.

Conclusion: Despite the use of relatively low biological doses respecting spinal cord constraints, SABR results in excellent 2 year local control rates with low morbidity. Through careful selection of patients with oligometastases, most patients are alive and free from widespread metastases at 2 years. This cohort warrants further investigation in clinical trials of SABR.

Key words: Intensity-modulated radiotherapy; metastasis; radiosurgery; spine; stereotactic body radiotherapy

Introduction

The term oligometastases describes an intermediate state of cancer spread between localised disease and widespread metastasis [1]. When patients develop metastases from solid tumours they are generally regarded as incurable [1]. However, long-term cures have been shown in patients with limited metastatic disease in various different cancers [2–4]. An attractive consequence of the concept of oligometastases is that some patients with metastatic disease may still be curable using local therapies.

Stereotactic ablative body radiotherapy (SABR) has been shown to be an effective, non-invasive alternative to surgery for treating oligometastases [1,5,6]. SABR refers to an external beam radiotherapy treatment that delivers a high biological dose of radiation with high geometric precision to an extra-cranial target, typically using one to five

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fractions, delivered using highly specialised planning and treatment delivery techniques [7]. There are multiple single cohort prospective studies and retrospective reviews of using SABR for the treatment of lung metastases, showing 2 year local control rates and overall survival rates of 90–100% and 50–70%, respectively [5,6,8]. Other body sites (including lung, liver, adrenal and lymph nodes) have also been treated with SABR, with local control rates ranging from 67 to 95% and 2–3 year survival rates in the range of 30–64% [1,9].

Evidence for the spine being an appropriate target for SABR is emerging. Multiple prospective cohort and retrospective studies have been carried out on SABR for spinal metastases, showing local control rates of about 80–90%, with low rates of toxicity [10,11]. However, most are in the context of patients with significant metastatic burden and few studies have examined the use of spinal SABR specifically in the setting of oligometastases. Spinal SABR has theoretical shortcomings compared with other body sites. Due to concerns about causing radiation myelopathy [12] and vertebral compression fractures (VCF) [13], prescribed doses for spinal SABR are typically lower than those used in other body sites such as the lung and liver. Moreover, at the interface between the planning target volume and the spinal cord, doses are typically compromised even further below the intended prescribed dose, in order to meet dose constraints for the spinal cord [12]. An example of a typical dose distribution achieved with spinal SABR, where the dose at the interface between the planning target volume and the spinal cord is lowered, is shown in Figure 1. This raises the possibility that treating spinal metastases with SABR may result in inferior outcomes to those reported in other sites in the body, where higher doses can be safely used.

The aim of this study was to evaluate the outcome of patients treated with spinal SABR in the oligometastatic setting. As patients with metastatic disease treated with local therapies are at significant risk of further distant relapse, we focused in particular on reporting patterns of failure in this cohort.

Materials and Methods

This was a multi-institutional retrospective review of patients with oligometastases undergoing SABR. Patients were recruited from Peter MacCallum Cancer Centre, Royal North Shore Hospital, Princess Alexandra Hospital and William Buckland Radiotherapy Centre. This study was approved by the institutional ethics committees of all four hospitals. Patients were included in this study if they were treated with spinal SABR between 1 January 2010 and 31 July 2014, and had oligometastases (defined as up to three metastases, all of which were treatable with extirpative or locally ablative treatment). Patients were excluded if they had more than three metastases at the time of SABR, had primary disease not treated with definitive intent or had a haematological primary malignancy. Patient data were collected until the study-wide closeout date of 30 June 2015.

Diagnostic magnetic resonance imaging scans were fused to planning computed tomography scans in all cases. Where possible, magnetic resonance imaging scans were carried out on a flat table top to aid fusion. Clinical target volumes were defined according to consensus guidelines [14]. SABR was delivered in one to three fractions using either fixed gantry angle intensity-modulated radiotherapy or volumetric-modulated arc therapy. Prescriptions were to covering isodoses, which varied between institutions, but were generally between 70 and 80%. SABR was prescribed to no more than three metastases in any treatment episode. The techniques for patient planning and treatment delivery varied between the four different institutions and are described in Table 1.

The primary objective was to characterise the widespread failure-free survival (WFFS). Widespread failure was defined as the development of metastatic disease not amenable to further locally ablative or extirpative therapy. WFFS was defined as the time from completion of SABR until widespread failure or death. We chose this as the primary end point to allow comparison with a previous study of SABR for oligometastases, which used a similar

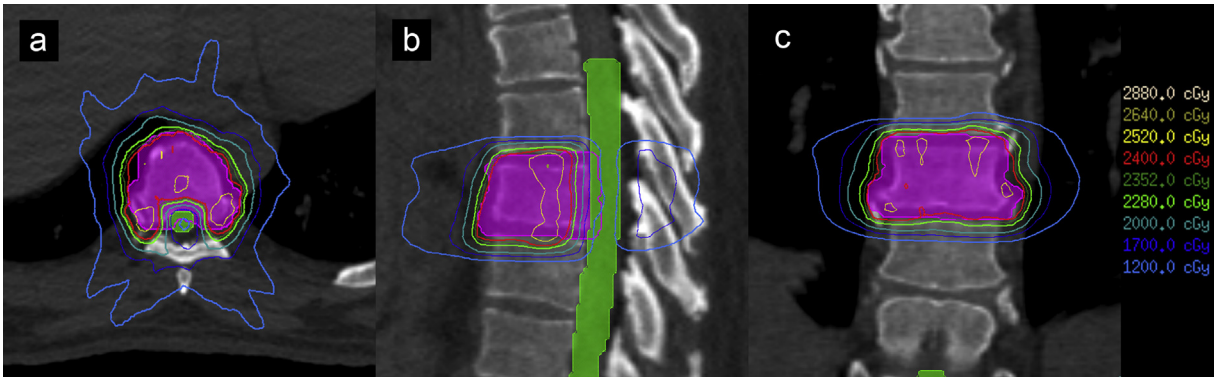

Fig 1. An example of a typical dose distribution achieved in a spine stereotactic ablative body radiotherapy plan prescribed to 24 Gy in two fractions with a spinal cord planning organ-at-risk limit of 17 Gy maximum point dose. The plan is shown on computed tomography, zoomed in on the target T8 vertebra, shown in axial (a), sagittal (b) and coronal (c) planes. The planning target volume is shown in pink colour wash and the spinal cord planning organ at risk volume is shown in green colour wash. The isodose lines are shown with the dose legend on the right.

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