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Original Article

Single Fraction Stereotactic Ablative Body Radiotherapy for Oligometastasis: Outcomes from 132 Consecutive Patients

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Abstract

Aims: Stereotactic ablative body radiotherapy (SABR) is currently used to treat oligometastases, but the optimum dose/fractionation schedule is unknown. In this study, we evaluated outcomes after single fraction SABR in patients with oligometastatic disease.
Materials and methods: Single institutional retrospective review of patients treated with single fraction SABR for one to three oligometastases between 2010 and 2015. The primary outcome was freedom from widespread disease defined as distant recurrence not amenable to surgery or SABR; or recurrence with four or more metastases.
Results: In total, 186 treatments were delivered in 132 patients. The two most common target sites were lung (51%) and bone (40%). The most frequent single fraction prescription dose was 26 Gy (47%). The most common primary malignancy was genitourinary ($n = 46$ patients). Freedom from widespread disease was 75% at 1 year (95% confidence interval 67–83%) and 52% at 2 years (95% confidence interval 42–63%). Freedom from local progression at 1 year was 90% (95% confidence interval 85–95%) and at 2 years was 84% (95% confidence interval 77–91%). A compression fracture of the lumbar vertebra was the only grade 3+ treatment-related toxicity.
Conclusions: Single fraction SABR is associated with a high rate of freedom from widespread disease, favourable local control and low toxicity comparable with historic multi-fraction SABR reports.

Key words: Oligometastases; radiotherapy; SABR; single fraction; stereotactic

Introduction

In 1995, Hellman and Weichselbaum [1] coined the term ‘oligometastases’ to describe a less-advanced state of metastatic disease, amenable to potentially curable local therapy such as surgery or radiotherapy. Treatment for oligometastases is challenging as there is always the competing risk of distant failure and it is this distant failure that often predominates the patient’s subsequent outcome. There is a widespread perception that most patients with oligometastases may develop multiple metastases in a short time, rendering ablative therapy of the oligometastatic disease futile.

The aim of this study was to review the clinical outcomes of patients with oligometastases treated with single fraction stereotactic ablative body radiotherapy (SABR) at our institution. As most patients with oligometastases are destined for further distant relapse, we postulated that a single session of treatment (if effective) would maximise patient convenience and resource utilisation. The primary objective was to describe the freedom from widespread metastasis [2,3], defined as metastatic disease not amenable to local therapy (i.e. resection or SABR), or the development of four or more new metastases at follow-up.

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From an international survey of physicians, the main reason for not using SABR for oligometastases is a perceived lack of evidence demonstrating clinical advantages. Furthermore, there is little consensus as to the SABR dose and fractionation prescribed in order to adequately inform evidence-based practice. For example, a single fraction of 20 Gy was among the top three prescriptions only in Western Europe [4]. The most common regimens were 50 Gy in five fractions, 48 Gy in four fractions and 30 Gy in five fractions. At our institution the referral pattern included many patients travelling great distances to attend the clinic, so we opted for a predominantly single fraction SABR approach for oligometastatic disease.

Materials and methods

This retrospective review received institutional ethics approval for the study of patients with oligometastases treated with SABR between February 2010 and March 2015. The data close-out date was March 2016. We included patients receiving single fraction SABR for one to three extracranial metastases only at the time of SABR. Prior local or systemic treatment for metastatic tumours was not an exclusion criterion. Patients who had distant progression after SABR with one to three metastases were routinely considered for further salvage SABR. All patients had had radical treatment to the primary cancer.

The primary objective was to assess the freedom from widespread disease (FFWD). The secondary objectives included describing freedom from local progression (FFLP), overall survival, freedom from distant progression (FFDP), rate of any treatment-related morbidity including grade 3+ toxicity using CTCAE v4.0. We also described the timing of initiation of systemic treatment following SABR. Systemic therapy included hormone and androgen deprivation therapy.

Statistical Considerations

FFWD was defined as metastatic disease not amenable to local therapy (i.e. resection or SBRT) or the development of four or more new metastases at the time of follow-up [2,3]. Death without widespread disease was considered a censoring event.

Local failure was documented with either a positive pathological diagnosis post-SABR or a radiological increase in size based on Response Evaluation Criteria In Solid Tumors (RECIST) criteria [5] with confirmation through positron emission tomography (PET). FFDP was defined as the time from the date of completion of treatment to the date of first distant progression. If the distant progression was without widespread disease then the lesions were considered for further treatment with SABR or surgery. Death was a censoring event for FFLP and FFDP. Treatment-related morbidity included all grades of toxicity. Severe toxicity was defined as a grade 3+ adverse event assessed using CTCAE V4.0.

Time to event outcomes were described using Kaplan–Meier methods with 95% confidence intervals. FFLP was assessed for each lesion. Overall survival, FFDP and FFWD variances were calculated using Greenwood's formula, whereas FFLP variance was assessed using Ying and Wei [6] formula to account for within-patient effect. Treatment-related morbidity and grade 3+ toxicities were described as cumulative incidence assuming competing risks, with death as a competing event.

Stereotactic Ablative Body Radiotherapy Technique

Magnetic resonance imaging and PET scans, where available, were fused with the planning computed tomography scan for improved delineation of the gross target volume. For lung metastasis, a motion encompassing the internal target volume (ITV) was created based on four-dimensional computed tomography. The planning target volume (PTV) expansion was usually 5 mm, except for spinal targets in which the PTV margin was 2 mm. Dose constraints to the spinal cord and other organs at risk were based on data from AAPM Task Group 101 [7]. Respiratory gating was not used. Cone beam computed tomography with online clinician review was the most common technique used for image guidance.

Intensity-modulated radiotherapy and three-dimensional conformal radiotherapy techniques were used with 6 MV photons. The conformal plans usually involved six to eight coplanar fields and one to two non-coplanar fields. Treatment was typically prescribed to the 80% isodose line covering the PTV. SABR dose was based on site, proximity to critical structures, size, histology, location and consensus at weekly SABR chart rounds. For example, 20 Gy for the spine, 18 Gy for centrally located lung tumours, 26/28 Gy for peripheral lung tumours, 20 Gy for bone metastases (breast and prostate) and 24 Gy for non-vertebral bone and soft tissue metastases. The planning objective was to achieve coverage of the PTV to D99% by the prescription isodose. A different objective was used in spine SABR with the goal of D90 = 90% to the PTV. All patients underwent individual patient quality assurance. Treatment planning was carried out with the computerised treatment planning system Eclipse (Varian Eclipse, Palo Alto, CA, USA) and iPlan (Brainlab, Germany). The dose distribution was calculated using Analytical Anisotropic Algorithm for Eclipse and pencil beam or Monte Carlo calculations for iPlan to account for tissue heterogeneities.

Follow-up

The follow-up protocol was clinical review and imaging carried out every 3–4 months in the first 2 years followed by 6 monthly imaging and clinic visits from years 3–5. This follow-up protocol was practised across all disease sites. The imaging findings, toxicity and grade were documented at every follow-up.

Results

In total, 132 patients had 186 lesions treated with single fraction SABR over 152 treatment courses. The median

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