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Clinical Study

Technique and early clinical outcomes for spinal and paraspinal tumours treated with stereotactic body radiotherapy

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ABSTRACT

We report technique and early clinical results of stereotactic body radiotherapy (SBRT) from Princess Alexandra Hospital. SBRT involves the precise delivery of highly conformal and image-guided external beam radiotherapy with high doses per fraction. It is increasingly being applied in management of spinal tumours. Thirty-six courses of spine SBRT in 34 patients were delivered between May 2010 and December 2013. Mean patient age was 58 years. Treatment was predominantly for metastatic disease, applied in *de novo* (n = 22), retreatment (n = 14) and postoperative (n = 8) settings. Prescribed doses included 18–30 Gy in 1–5 fractions. SBRT technique evolved during the study period, resulting in a relative dose escalation. No severe acute toxicities were observed. At median follow-up of 7.4 months (range: 1.7–22.2), no late radiation myelopathy was observed. Risk of new/worsening vertebral compression fractures was 22% (n = 8) and was significantly associated with increasing Spinal Instability Neoplastic Scores ($p = 0.0002$). In-field control was 86% with relapse occurring at a median interval of 2.8 months (range: 1.9–4.7). Thirteen patients (36%) died and median overall survival has not been reached. SBRT is an evolving technology with promising early efficacy and safety results. The outcomes of this series are comparable with international literature, and await longer follow-up.

1. Introduction

Stereotactic body radiotherapy (SBRT) involves the precise delivery of highly conformal and image-guided hypofractionated external beam radiotherapy to an extracranial target [1,2]. Large doses are delivered in a single or small number of fractions (typically one to five), resulting in a high biologic equivalent dose (BED) to the tumour [3,4]. Sparing of proximal normal tissues requires sophisticated planning techniques which generate steep dose gradients adjacent to the target. To ensure accurate treatment delivery, careful attention must be paid to patient immobilisation and image guidance.

SBRT is increasingly being applied in the management of benign and malignant spinal and paraspinal tumours [4–8]. *De novo* spinal SBRT aims to improve local control in the management of oligometastases, patients of good performance status with bone only metastatic disease, and for tumours considered resistant to conventional fractionation (for example, renal cell carcinoma and melanoma) [4,9,10]. Efficacy of SBRT has also been demonstrated in the setting of previous spinal radiotherapy or following debulking/stabilisation surgery [11,12].

Princess Alexandra Hospital introduced a program of spinal SBRT in early 2010. We describe our initial experience, including treatment technique and early clinical outcomes.

2. Methods

All patients treated with SBRT for spinal and paraspinal disease at the Princess Alexandra Hospital up to December 2013 were reviewed. Both primary tumours and metastases were included. Clinical information relating to presenting features, previous treatment, staging and follow-up of outcomes was obtained through review of medical records, correspondence from other providers and medical imaging. Treatment technique and plan dosimetry

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was reviewed for all cases. Data was recorded in a de-identified manner, following Institutional Ethics Board approval.

2.1. SBRT technique

Patients were immobilised using customised devices (thermoplastic masks and vacuum cushions) with analgesic and anxiolytic medications prescribed as required. A planning CT scan was co-registered with diagnostic MRI sequences (or CT myelogram in postoperative patients with significant high density artefact). The gross tumour volume (GTV) encompassed all radiographically apparent tumour. The clinical target volume included suspected microscopic disease extension and was a 5mm expansion on extra-osseous GTV and an anatomical expansion on osseous GTV, in keeping with international consensus guidelines [13]. Further 2–3 mm planning target volume (PTV) and planning organ at risk volume expansions were applied to account for positional error and other uncertainties, as previously described [2].

A range of dose prescriptions were used, depending on the volume of disease and complexity of target, commonly 20 Gy in a single fraction or 24–28 Gy in 2–3 fractions. Planning technique evolved over the study period with early treatments predominantly employing intensity modulated radiotherapy with 9–11 static fields prescribed to a reference point. Later treatments were planned using volumetric modulated arc treatment using two coplanar arcs prescribed to a covering isodose.

Maximum point dose to the spinal cord planning organ at risk volume/thecal sac (SC PRV/TS) was adapted according to number of SBRT fractions, previous radiotherapy dose and accepted probability of myelopathy [14–16]. PTV coverage was compromised in order to meet SC PRV/TS dose constraints whilst aiming to keep the dose received by 90% of the PTV (D90) greater than 80–90% of the prescription dose. Hot spots of up to 140% of the prescription dose were accepted provided they remained within optimised PTV and $\geqslant$5 mm from SC PRV/TS.

All patients were presented at a biweekly departmental SBRT quality assurance meeting where the clinical indications for SBRT and proposed treatment plan were reviewed. Physics quality assurance was performed for every plan prior to treatment using phantom dose measurements on the treatment machine.

SBRT was delivered using an Elekta Axesse linear accelerator (Elekta, Stockholm, Sweden) with 4 mm multileaf collimator to shape the treatment beam and vary dose intensity. Image guidance utilising cone beam CT scan was performed in order to minimise inter- and intrafraction positional error. The introduction of a robotic couch allowed correction of positional errors in six degrees of freedom (HexaPOD; Medical Intelligence, Schwabmünchen, Germany).

2.2. Outcome measures

Patients were clinically assessed 4–6 weeks post treatment and then at 3 monthly intervals with repeat imaging. Where patients came from remote locations or were too unwell to travel, follow-up was performed by local providers and outcome data was obtained from correspondence.

Local relapse (LR) was defined as progression based on tumour growth on imaging and/or clinical findings such as worsening of pain or neurological symptoms, in the absence of vertebral compression fracture as an explanation for these symptoms. Pathological vertebral compression fracture (VCF) was assessed radiographically as $\geqslant$10% reduction in vertebral height. Spinal stability as assessed using the Spinal Instability Neoplastic Score (SINS) [17]. Toxicity was graded according to Common Terminology Criteria for Adverse Events version 3.0. (Cancer Therapy Evaluation Program, National Institutes of Health, USA). As some patients received more than one course of spinal SBRT, overall survival was calculated from commencement of first spinal SBRT course until last known follow-up or death.

2.3. Statistical analyses

Descriptive statistics were reported as median and range for continuous variables and frequencies and proportions for categorical variables. Mann–Whitney test and two-tailed Fischer's exact test were used to compare clinical and dosimetric parameters with overall survival, local relapse or compression fracture. Results were adjusted for multiple comparisons using a false discovery rate (FDR) of < 5%. Statistical analyses were performed using GraphPad Prism (version 6.0; GraphPad Software, San Diego, CA, USA).

3. Results

3.1. Patient Characteristics

Thirty-six courses of spine SBRT in 34 adult patients were delivered between May 2010 and December 2013. Mean patient age was 58 years (range: 29–81). Patient characteristics are summarised in Table 1.

Table 1
Characteristics of patients treated with stereotactic body radiotherapy

Characteristic	Parameter	n	%
Performance status	ECOG		
	0	6	17.6
	1	24	70.6
	2	3	8.8
	3	1	2.9
	4	0	0
Histology	Primary		
	Plasmacytoma	1	2.9
	Sarcoma	1	2.9
	Metastatic		
	Melanoma	8	23.5
	Prostate adenocarcinoma	8	23.5
	Breast adenocarcinoma	6	17.6
	Other	9	35.4
Extent of extra-spinal disease	Nil	14	41.2
	Bone only metastases	4	11.8
	Visceral metastases	16	47.0
Local symptoms	Nil	9	25.0
	Any pain	22	61.1
	Pain requiring opiate analgesia	13	36.1
	Neurologic deficit	4	11.1
Spinal stability[†]	Stable (SINS 0–6)	15	51.7
	Potentially unstable (SINS 7–12)	14	48.3
	Unstable (SINS 13–18)	0	0
Number of vertebral bodies involved	1	28	77.8
	2	5	13.8
	3	3	8.3
Spinal level	Cervical	4	11.1
	Thoracic	15	41.7
	Lumbar	15	41.7
	Overlapping	2	5.5
Previous local radiotherapy	Yes	14	38.9
	No	22	61.1
Indication	Definitive	28	77.8
	Post-operative		
	Adjuvant	1	2.8
	Residual disease	5	13.9
	Recurrent disease	2	5.5

ECOG = Eastern Cooperative Oncology Group Performance Status Score, SINS = Spinal Instability Neoplastic Score.
[†] Excluding patients with prior stabilisation surgery.