Practical Radiation Oncology (2014) 4, e143–e149

practical radiation oncology
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Original Report

Outcomes and toxicities of stereotactic body radiation therapy for non-spine bone oligometastases

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Received 28 March 2013; revised 20 May 2013; accepted 22 May 2013

Abstract

Purpose: Stereotactic body radiation therapy (SBRT) is being applied more widely for oligometastatic disease. This technique is now being used for non-spine bony metastases in addition to liver, spine, and lung. However, there are few studies examining the toxicity and outcomes of SBRT for non-spine bone metastases.

Methods and Materials: Between 2008 and 2012, 74 subjects with oligometastatic non-spine bony metastases of varying histologies were treated at the Mayo Clinic with SBRT. A total of 85 non-spine bony sites were treated. Median local control, overall survival, and progression-free survival were described. Acute toxicity (defined as toxicity <90 days) and late toxicity (defined as toxicity ≥ 90 days) were reported and graded as per standardized Common Toxicity Criteria for Adverse Events 4.0 criteria.

Results: The median age of patients treated was 60 years. The most common histology was prostate cancer (31%) and most patients had fewer than 3 sites of disease at the time of simulation (64%). Most of the non-spine bony sites lay within the pelvis (65%). Dose and fractionation varied but the most common prescription was 24 Gy/1 fraction. Local recurrence occurred in 7 patients with a median time to failure of 2.8 months. Local control was 91.8% at 1 year. With a median follow-up of 7.6 months, median SBRT specific overall survival and progression-free survival were 9.3 months and 9.7 months, respectively. Eighteen patients developed acute toxicity (mostly grade 1 and 2 fatigue and acute pain flare); 9 patients developed grade 1-2 late toxicities. Two patients developed pathologic fractures but both were asymptomatic. There were no late grade 3 or 4 toxicities.

Conclusions: Stereotactic body radiation therapy is a feasible and tolerable treatment for non-spine bony metastases. Longer follow-up will be needed to accurately determine late effects.

Conflicts of interest: None.

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1879-8500/$ – see front matter
http://dx.doi.org/10.1016/j.prro.2013.05.006

Introduction

An important component of a clinical radiation oncology practice is the treatment of painful bony metastases. Multiple randomized trials have shown that external beam radiation with a single 8 Gy fraction is effective for pain control although the need for retreatment is more frequent when compared with stereotactic higher doses.[1,2] However, local control has evolved into a salient issue in recent years as improved systemic therapies has led to longer survival in cancer patients with metastatic disease. Prior to stereotactic body radiation therapy (SBRT), patients with good performance status frequently received doses up to 30 Gy/10 fractions.[3] SBRT provides the capability of delivering precise high-dose radiation (biologic equivalent doses that are 2-3 times higher than the equivalent dose provided by 30 Gy/10 fractions) to oligometastatic disease, which may improve quality of life by extending the duration of pain control and delaying disease progression while reducing local side effects and the need for reirradiation.[4,5] For radioresistant tumors such as melanoma and renal cell carcinoma, SBRT may offer improved local control with fewer late effects.[6-8] For patients who have no symptoms at the time of SBRT delivery, the role of SBRT may be to defer initiation of systemic therapy by controlling local disease.

Multiple studies have been published on spinal and vertebral body SBRT as a salvage treatment for recurrent vertebral disease and cord compression.[9-11] There are phase 2 trials under way to examine its role as first line treatment for cord compression and spinal bone metastases in a highly selected group of patients (Radiation Therapy Oncology Group 0631; Princess Margaret Hospital trial/ MD Anderson Cancer Center trial). In contrast, there is a very little literature on the use of SBRT for non-spine bony metastases. A recent survey of radiation oncology practice in North America showed that SBRT is increasingly being adopted for the treatment of a number of oligometastatic sites including non-spine bony metastases[12]; yet the optimal dose and late effects such as fracture risk and osteoradionecrosis remain unknown.

The current study examines the Mayo Clinic experience treating patients with SBRT to non-spine bony metastasis.

Methods and materials

The Mayo Clinic has prospectively assessed, treated, and followed 74 patients from January 1, 2008 to August 1, 2012 with SBRT for non-spine bony metastases. Information was collected on patient age, sex, histology, bony site treated, pain relief, number of metastases at simulation, whether the treated site had previously received radiation therapy, local control, distant progression, radiographic response to treatment, SBRT prescription dose, chemotherapy delivery, and acute and late toxicity. Descriptive statistics were performed using JUMP (version 9.01; SAS Institute Inc, Cary, NC). Median progression-free survival, overall survival, and follow-up from the end of SBRT treatment were also calculated. Progression-free survival was defined as any progression (local or distant) from the end of SBRT treatment. Local failure was defined as in-field progression over serial imaging with computed tomographic (CT) scan, magnetic resonance imaging (MRI), and when available, positron emission tomography (PET)-CT. This study was approved by the Mayo Clinic institutional review board ethics board. Local control was defined as stable disease, partial response, or complete response based on serial imaging with CT scan, MRI, or PET-CT. A complete response was coded if there was complete disappearance of [^{18}F]fluoro-2-deoxy-2-d-glucose-avidity on PET-CT or complete resolution of the tumor on CT scan or MRI.

Patients were immobilized using a 5 point mask for lesions above the T3 vertebral level and the commercially available BodyFix system (Electa AB, Stockholm, Sweden) for lesions below the T3 vertebral level. While we did perform 4-dimensional (4D)CT for some rib lesions, our experience was that the internal target volume did not change appreciably from the gross tumor volume (GTV) so this was not routinely performed. 4DCT was required for sternal lesions as there was significant anterior–posterior movement with respiration, although breath hold or gating was not routinely used for these lesions. Radiation therapy was delivered on a daily basis for fractionated regimens.

The SBRT plans were designed using Eclipse (Varian, Palo Alto, CA) treatment planning software. Generally, most patients had intensity modulated RT or volumetric modulated arc therapy techniques used to treat their bone lesions. The GTV was defined as the gross visible lesion on diagnostic PET-CT, CT scan, or MRI. The clinical target volume (CTV) encompassed the GTV plus 1 cm of contiguous bone and soft tissue extension if present. The planning target volume (PTV) included the CTV plus a 2-mm margin. The GTV was then expanded by 0 mm to be a high-dose PTV (range of doses, 16-24 Gy) and a low-dose PTV (range of doses, 14-18 Gy) was generated by expanding the CTV as defined previously. The dose was prescribed to cover the PTV by the 95% isodose line. Depending on location, adjacent normal tissue organs at risk were defined and kept below dose constraints as reported in TG101.[13]

Imaging was performed with the ExacTRAC 6D x-ray system (Brainlab, Felkirchen, Germany) with the 6D robotic couch. Corrections were applied and full verification imaging using both tube detector pairs was repeated to confirm positioning within 1-2 mm and 1 degree. Before delivering each treatment field, a "Snap" verification image using a single tube detector pair was acquired. Shifting occurred if the Snap verification image was greater than 2 mm. If necessary, a pair of kV orthogonal images or cone-beam CT was obtained to verify the isocenter.