Clinical Oncology 25 (2013) 236–241

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Lung Metastases Treated with Image-guided Stereotactic Body Radiation Therapy☆

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Received 6 June 2012; received in revised form 28 November 2012; accepted 4 December 2012

Abstract

Aims: To evaluate outcomes after treatment with image-guided stereotactic body radiation therapy (SBRT) using daily online cone beam computed tomography for malignancies metastatic to the lung.

Materials and methods: Forty-seven lung metastases in 32 patients were treated with volumetrically guided SBRT. The median age was 62 years (21–87). Primaries included colorectal ($n = 10$), sarcoma ($n = 4$), head and neck ($n = 4$), melanoma ($n = 3$), bladder ($n = 2$), non-small cell lung cancer ($n = 2$), renal cell ($n = 2$), thymoma ($n = 2$), thyroid ($n = 1$), endometrial ($n = 1$) and oesophageal ($n = 1$). The number of lung metastases per patient ranged from one to three (68% single lesions). SBRT was prescribed to the edge of the target volume to a median dose of 60 Gy (48–65 Gy) in a median of four fractions (four to 10). Most lesions were treated using 12 Gy fractions (92%) to 48 or 60 Gy.

Results: The median follow-up was 27.6 months (7.6–57.1 months). The 1, 2 and 3 year actuarial local control rates for all treated lesions were 97, 92 and 85%, respectively. Two patients with colorectal primaries (four lesions in total) had local failure. The median overall survival was 40 months. The 1, 2 and 3 year overall survival from the time of SBRT completion was 83, 76 and 63%, respectively. There were no grade 4 or 5 toxicities. Grade 3 toxicities (one instance of each) included pneumonitis, dyspnoea, cough, rib fracture and pain.

Conclusion: SBRT with daily online cone beam computed tomography for lung metastases achieved excellent local tumour control with low toxicity and encouraging 2 and 3 year survival.

Key words: Lung metastases; oligometastases; SBRT; stereotactic body radiation therapy

Introduction

Patients with oligometastases are now being considered candidates for curative therapy. Metastases to the lungs are common and remain a challenge in many patients with different primary malignancies. In patients without evidence of widespread extrapulmonary disease, studies have shown that pulmonary metastasectomy can prolong survival and cure some patients [1–3]. Surgical resection is considered the standard of care in those who have resectable disease, can tolerate surgery, and have controlled extrapulmonary disease. However, for those patients where surgery is not feasible, treatment options are limited.

Stereotactic body radiation therapy (SBRT) is an emerging treatment modality that can potentially offer local control and long-term overall survival. In contrast to standard fractionated radiation therapy, SBRT uses high-dose, hypofractionated irradiation to target small volumes. SBRT can be given in one to five fractions versus 30–37 fractions with standard external beam radiation therapy, using multiple beam angles and a three-dimensional conformal technique.

SBRT has been extensively studied in stage I non-small cell lung cancer, predominantly in the medically inoperable, where it has been shown to have excellent control rates and achieve long-term survival [4,5]. It is well tolerated and can be safely administered with low morbidity [6].

☆ Presented in poster form at the 52nd Annual Meeting of the American Society for Radiation Oncology, 31 October–4 November 2010, San Diego, California, USA.

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0936-6555/$36.00
http://dx.doi.org/10.1016/j.clon.2012.12.005

There have been very few studies examining the role of SBRT for the treatment of lung metastases. In this study, we report our results of patients treated with SBRT for lung metastases, including a subset of patients who were on a prospective study.

Materials and Methods

Patient Characteristics

From May 2007 to May 2011, 32 patients with 47 lung metastases were treated with image-guided SBRT using daily online cone beam computed tomography (CBCT). Nine patients were enrolled on a prospective in-house phase II SBRT trial; the remaining 23 had data analysed retrospectively from a prospective database. These 23 patients were either ineligible or refused to participate in the phase II protocol. However, their outcome and toxicity data were collected at each follow-up visit and entered into a database. Any missing data were obtained retrospectively. The study was approved by the William Beaumont Hospital institutional review board (HIC# 2011-311).

Eligibility for patients enrolled on the prospective trial included medically inoperable adult patients with one to three lung metastases, $\leq$5 cm in size. Patients with extrathoracic disease were eligible as long as their primary tumour and extrathoracic metastases were controlled. Patients with prior lung surgery, lung irradiation, systemic chemotherapy or current systemic chemotherapy were all eligible; however, a 6 week period between systemic therapy and SBRT was recommended and required for all protocol patients. Patients who were not enrolled on the trial and underwent SBRT required similar inclusion criteria: one to three lung metastases, controlled extrathoracic disease and medically inoperable or refusing surgery. All patients had biopsies of their metastatic lung lesions proving metastatic disease before SBRT. All patients were initially evaluated with a history and physical examination (including evaluation by an experienced thoracic surgeon), chest computed tomography and ^{18}F-fluorodeoxyglucose positron emission tomography computed tomography (^{18}FDG PET-CT), and pulmonary function tests.

Stereotactic Body Radiation Therapy Technique

The SBRT treatment planning and delivery methods at our institution have previously been described [4,7]. Briefly, patients were immobilised during computed tomography simulation in a stereotactic body frame (Elekta Oncology, Norcross, Georgia, USA), Body Fix (Elekta Oncology), alpha-cradle (KGF Enterprises, Chesterfield, Michigan, USA) or modified alpha-cradle/BodyFix hybrid device. Four-dimensional computed tomography (Philips Clinical System, Madison, Wisconsin, USA) and free-breathing computed tomography were carried out in all patients. Abdominal compression was used in five patients (16%) with tumour excursion more than 1.0 cm. Computed tomography data were transferred to the planning workstation (Pinnacle v7.4f; Philips, Milpitas, California, USA), registered, and fused with a planning PET. SBRT plans consisted of six to nine coplanar and non-coplanar beams with a limited number of couch angles. Static single-segment beams, optimised with the Pinnacle software Direct Machine Parameter Optimization were typically used; multi-segment intensity modulated radiation therapy was used in some patients in order to meet normal tissue dose–volume constraints.

The gross tumour volume (GTV) equalled the tumour on computed tomography lung windows with consideration of the registered PET. The internal target volume (ITV) was composed of the union of the GTV defined in 10 phases of respiration, rendering an ITV = $GTV_{phase1} \cup GTV_{phase2} \ldots \cup GTV_{phase10}$. The clinical target volume was the ITV plus a 4 mm three-dimensional expansion. The planning target volume (PTV) required a 5 mm three-dimensional expansion of the clinical target volume. The dose was prescribed to the PTV edge (typically 80% isodose line, range 60–90%). On protocol, patients were treated to a dose of 60 Gy in five fractions. The protocol did not differentiate between central and peripheral tumours. Tumours within 2 cm of the proximal bronchial tree were eligible if dose–volume histogram constraints for the proximal bronchial tree were achievable (maximum point dose: 34 Gy, four fractions; 37.5 Gy, five fractions). The rest of our dose–volume histogram constraints have been previously published [4]. For off protocol patients, the same protocol dose constraints were used, but fractionation size and dose were based on tumour size and location. Overall, the median dose prescribed was 60 Gy (48–65 Gy) in a median of four fractions (between four and 10). Most lesions were treated using 12 Gy fractions (92%) to 48 or 60 Gy (Table 1). Treatment was typically administered once every other day with a minimum of 40 h and a maximum of 4 days between fractions. Patients who had multiple metastatic lesions treated had their SBRT delivered sequentially. Daily online CBCT-based volumetric image-guided radiation therapy using soft tissue target registration was applied immediately before all SBRT deliveries. Three CBCTs were carried out per fraction: before correction, after correction, and after fraction delivery. Decadron 4 mg orally was given before each fraction.

Table 1
Dose fractionation schemes

Dose (Gy)/fractions	
60/5	36 (77%)
48/4	7 (15%)
50/5	1 (2%)
60/10	2 (8%)
65/10	1 (2%)
Dose (Gy) per fraction	
12	43 (92%)
10	1 (2%)
6.5	1 (2%)
6	2 (4%)