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Early and late lung radiographic injury following stereotactic body radiation therapy (SBRT)

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ABSTRACT

Objective: To describe early and late CT patterns of radiographic lung injury after SBRT for lung cancer, and to correlate radiological findings with patient and treatment characteristics.
Materials and methods: Follow-up CT scans of 68 patients with 70 tumors were divided into 4 periods: (1) 6 weeks; (2) 2–6 months; (3) 7–12 months and (4) 13–18 months after SBRT. Early (within 6 months) and late radiological injuries were evaluated according to Ikezoe and Koening, respectively. The correlation between CT findings and patient characteristics was evaluated.
Results: Radiographic injury in periods 1 and 2 was: (1) diffuse consolidation 3 and 27%, (2) patchy consolidation and ground-glass opacity (GGO) 13.2 and 33%, (3) diffuse GGO 13.2 and 21%, (4) patchy GGO 16.2 and 6%, and (5) no findings 54.4 and 21%, respectively. Late injury in periods 3 and 4 were: (1) modified conventional pattern (consolidation, volume loss, bronchiectasis) 54 and 44%, (2) mass-like 20 and 28%, (3) scar-like 14 and 16% and (4) no findings 20 and 12%, respectively. The proportion of emphysema grades 2–4 was significantly higher in patients who had no radiological findings 6 weeks after treatment ($p = 0.021$). Both patchy consolidation and GGO patterns resulted more frequently in patients who were not administered steroids ($p = 0.035$). No relationship was found with smoking, tumor dimension and radiation dose.
Conclusions: The majority of patients had no evidence of radiographic lung injury 6 weeks after SBRT; the most prevalent findings were diffuse or patchy GGO. Patchy and diffuse consolidation develops 2–6 months after SBRT. Modified conventional pattern was the most prevalent in the late periods.

1. Introduction

Stereotactic body radiation therapy (SBRT) is a recently introduced technique that allows the delivery of a very high radiation dose to the target volume, while minimizing the dose to the adjacent normal tissues. SBRT uses multiple planar and non-coplanar beams to generate a dose distribution that conforms tightly to the target volume. Whereas three-dimensional (3D)-conformal radiation therapy for lung cancer generally consists in 6/7 weeks of treatment, SBRT assumes a hypofractionated scheme, delivering the dose typically in 3–5 fractions; thus a high-dose per fraction is employed, typically 10–20 Gy/fraction, contrary to conventional fractionation schedule (2 Gy/fraction).

Surgery remains the standard therapy for operable patients with stage I non-small cell lung cancer (NSCLC). However, SBRT has been shown to be highly effective in the treatment of non-operable stage I lung cancer or lung metastases, with reported local control rates of 80–95% [1–8]. Considering these excellent results, it might be expected that an increasing number of patients will be treated with this technique.

The complex distribution of radiation dose of SBRT to the target volume and to the adjacent organs, the multiple beams employed, and the very high-dose per fraction can result in patterns of lung injury that are different than those of conventional 3D-conformal radiation therapy. Understanding these changes becomes even more crucial for patients who have operable lung cancer. Though SBRT has been used mainly in patients who do not have a surgical option, the ability to distinguish reactive change versus tumor recurrence will play a larger role in those with an option for surgical salvage. Therefore, it is important to describe the radiological

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changes that can occur as consequence of hypofractionated lung SBRT.

The purpose of our study is to describe the early and late patterns of radiographic lung injury on CT images after hypofractionated SBRT for primary and metastatic lung cancer, and to correlate the radiological CT findings to patient and treatment characteristics.

2. Materials and methods

Between June 2004 and July 2007, 73 consecutive patients underwent SBRT for primary NSCLC or lung metastases, and received their radiological and clinical follow-up at our institution. With the approval of our Institutional Review Board and after obtaining informed consent from each patient, we prospectively collected patient and tumor characteristics. The relative CT scans were retrospectively reviewed.

To be eligible for this analysis, patients must have been treated with SBRT and must have been followed with chest CT at our institution. Further inclusion criteria included the availability of the pre-treatment CT of the chest, for comparison. Patients treated for a relapsing tumor after wedge resection ($n = 4$) or after conventional radiation therapy ($n = 1$) were excluded from the study.

Sixty-eight patients, with 70 lung tumors, fulfilled our selection criteria. Two patients had two primary lung cancers each: one patient had two synchronous tumors that were treated in the same radiation session. The other patient developed two metachronous primary lung cancers – both treated with SBRT – within an interval of 8 months. Demographic data and tumor characteristics are listed in Table 1. Patients treated for primary NSCLC were considered inoperable because of the advanced age, poor performance status (PS), severe comorbidities or poor lung function. Metastatic patients underwent SBRT if they were in good medical condition, had one or two peripheral lung metastases, and had stable systemic disease. Histologic confirmation was obtained for all the lesions except 17 (24%): 19 lesions were adenocarcinomas, 14 squamous cell carcinomas, 17 non-small cell lung cancer not otherwise specified, and 3 metastases (melanoma, head and neck carcinoma and lung cancer metastases). Fifteen primary lung cancers and 2 metastases were treated based on clinical suspicion. Each of these were FDG-avid on PET or PET/CT scanning and were either unable to be biopsied (primary lung cancers) or had documented evidence of metastatic disease elsewhere. One patient with stage T4 had a satellite nodule within the lobe containing the primary tumor, and the two lesions were included in the same planning target volume.

Treatment planning for radiation was performed by immobilizing patients by Stereotactic Bodyframe (SBF, Elekta, Crawley, England), or BodyFix (Medical Intelligence, Munich, Germany), on the CT scanner. For patients treated with BodyFix, a complete 4DCT of the thorax was obtained for treatment planning. For patients treated with SBF, an initial limited-field 4DCT was obtained in order to determine the longitudinal dimension of tumor excursion during quite respiration. Diaphragm compression was employed for SBF immobilization if the tumor excursion was greater than 5 mm in cranio-caudal direction. Thus the diaphragm compression was employed in 27 patients (40%). 4DCT was then repeated for SBF patients to include the entire lung volume, for delineation of tumor and normal tissues. Our method for tumor delineation for SBRT using maximum intensity projection (MIP) was previously described [9]. An Internal Target Volume (ITV) was contoured by the treating radiation oncologist, as previously described [9]. The planning target volume (PTV) included an additional margin of 10 mm in cranio-caudal direction and 5 mm in the axial directions to the ITV. The maximum GTV diameter ranged from 11 to 45 mm, corresponding to a median volume of 20 cm^3 (range 2.1–110 cm^3). The median PTV was 34.7 cm^3 (range 3.6–235 cm^3). SBRT was performed using multiple [9–12] coplanar and non-coplanar beams, as shown in Fig. 1. The majority ($n = 59$, 84%) of tumors received a dose of 54–60 Gy in 3 fractions. Eleven lesions were treated with a dose of 45–48 Gy, delivered in 3–6 fractions; six of these lesions were located centrally [13]. Dose calculation were corrected for tissue inhomogeneity using the superposition/convolution algorithm, except for patients treated on the Radiation Therapy Oncology Group (RTOG) protocol 0236 ($n = 15$), that did not allow heterogeneity corrections. Patients on this protocol received 60 Gy given in 3 fractions. Generally, the radiation dose was prescribed to the 85% isodose-line, meaning the center of the target received a dose that is 15% higher than the prescribed dose. Normal tissue dose constraints for both RTOG 0236 and 0618 were adopted as our institutional dose constraints. Verification of treatment was performed by CT for every treatment prior to therapy. The majority of these were performed using cone-beam CT on our linear accelerator (67%). Treatment was delivered using 6-MV photons (Trilogy, Varian Medical System, Palo Alto, CA or Elekta, Crawley, England). Patients who were treated on the RTOG protocol ($n = 15$) were administered steroids preventively (dexamethasone 4 mg p.o. 15–60 min before each radiation fraction). Patients who were not treated on RTOG protocol were not prescribed steroids.

A total of 227 CT scans were obtained consisting of 68 base line and 159 follow-up studies. The CT examinations were performed using different multidetector (4-64) scanners (Somatom

Table 1
Patient ($n = 68$) and tumor ($n = 70$) characteristics.

Age	71 (49–93)
Gender	
Male	31
Female	37
Race	
White	60
Black	8
PS	
0	9
1	23
2	31
3	5
Smoker	
Y	45
N	23
Emphysema	
Y	43
N	25
Primary lung cancer	
T1	51
T2	12
T3	1
T4	1
Metastatic lung cancer	
Larynx	1
H&N	1
Melanoma	1
NSCLC	2
Tumor location	
Peripheral	64
Central	6
PTV dimension (cm^3)	34.7 (3.6–235)
Dose	
54–60 Gy/3 fractions	59
45–48 Gy/3–6 fractions	11
Steroids administration before radiation	
Y	15
N	55

Abbreviations. PS: performance status according to Zubroid. PTV: planning target volume.