

Physics Contribution: Clinical Physics

Retrospective Cohort Study of Bronchial Doses and Radiation-Induced Atelectasis After Stereotactic Body Radiation Therapy of Lung Tumors Located Close to the Bronchial Tree

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Summary

Atelectasis has been observed after SBRT of tumors close to the bronchial tree. In this retrospective study, the relationship between incidence of atelectasis and bronchial dose parameters was evaluated with survival analysis models, for patients treated with SBRT for tumors close to main, lobar, or segmental bronchi. A significant dose–response relationship

Purpose: To evaluate the dose–response relationship between radiation-induced atelectasis after stereotactic body radiation therapy (SBRT) and bronchial dose.

Methods and Materials: Seventy-four patients treated with SBRT for tumors close to main, lobar, or segmental bronchi were selected. The association between incidence of atelectasis and bronchial dose parameters (maximum point-dose and minimum dose to the high-dose bronchial volume [ranging from 0.1 cm³ up to 2.0 cm³]) was statistically evaluated with survival analysis models.

Results: Prescribed doses varied between 4 and 20 Gy per fraction in 2-5 fractions. Eighteen patients (24.3%) developed atelectasis considered to be radiation-induced. Statistical analysis showed a significant correlation between the incidence of radiation-induced atelectasis and minimum dose to the high-dose bronchial volumes, of which 0.1 cm³ (D_{0.1cm³}) was used for further analysis. The median value of D_{0.1cm³} ($\alpha/\beta = 3$ Gy) was EQD_{2,LQ} = 147 Gy₃ (range, 20-293 Gy₃). For patients who developed atelectasis the median value was EQD_{2,LQ} = 210 Gy₃, and for patients who did not develop atelectasis, EQD_{2,LQ} = 105 Gy₃. Median time from treatment to development of atelectasis was 8.0 months (range, 1.1-30.1 months).

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between the incidence of atelectasis and the dose to the high-dose volume of the bronchi is shown.

Conclusion: In this retrospective study a significant dose–response relationship between the incidence of atelectasis and the dose to the high-dose volume of the bronchi is shown. © 2013 Elsevier Inc.

Introduction

Stereotactic body radiation therapy (SBRT) is a standard treatment for inoperable stage I peripheral lung tumors, with many phase 2 trials and retrospective series reported in the literature with excellent local control and limited toxicity (1-4). However, there are uncertainties with this method for more centrally located tumors, owing to risk of toxicity. A phase 2 study reported by Timmerman et al (5) described excessive pulmonary toxicity, including 6 grade 5 toxicities out of 70 patients. The 4-year follow-up results from this study (6) showed grade 3-5 toxicity in 6 of 22 patients with central tumors. However, Haasbeek et al (7) and Nuytens et al (8) treated centrally located lung tumors with SBRT with an increased number of fractions, without any reported grade 4-5 toxicities. Several other studies report on SBRT for centrally located lung tumors and airway toxicity (9-12), but with little data on delivered bronchial doses. Kelsey et al (13) reported on bronchial doses and airway toxicity, and Miller et al (14) reported a dose–response relationship for bronchial stenosis, both after treatment with high-dose RT with conventional fractionation. In another study Unger et al (15) described doses to mainstem bronchi in patients with hilar tumors treated with the CyberKnife stereotactic RT system.

Radiation-induced damage of the bronchi may lead to stenosis, fibrosis and, depending on the extent of the changes and the airway diameter, to atelectasis (a complete or partial collapse of the lung structure). How much atelectasis affects the patient depends on their lung function and general condition. A partial collapse might not even be clinically noticeable.

The purpose of the present work was to evaluate the dose–response relationship between radiation-induced atelectasis and bronchial dose, from a retrospectively reviewed cohort of patients treated with SBRT for tumors located close to the bronchial tree. We attempted to determine a dose limit for the central airways when using SBRT.

Methods and Materials

Patient selection criteria

This retrospective cohort study included 104 patients with 185 tumors located approximately within 2 cm from the bronchial tree. Patients were treated with SBRT, including hypofractionation with 2-5 fractions, at Karolinska University Hospital in Stockholm (May 1994 to March 2004) or Sahlgrenska University Hospital in Gothenburg (March 2000 to December 2005). The inclusion criteria were patients with medically inoperable stage I non-small cell lung cancer (NSCLC), or patients with 1 or a few lung metastases from any malignancy, good performance status, and relatively long life expectancy. The study was approved by the ethics committee. Two specialists in lung cancer oncology screened all the patient records, radiology reports, and computed tomography (CT) studies. Diagnostic CT examinations (generally

with contrast) made before and after RT were also evaluated by thoracic radiology specialists. The aim was to evaluate treatment-related toxicity with respect to atelectasis in partial, segmental, lobar, or whole lung. Therefore, atelectasis caused by radiation and by progressing tumor was discriminated. Local progression was diagnosed by bronchoscopy with biopsy. If that not was possible to perform, a positive result on positron emission tomography–CT was mandatory. Excluded from the analysis were 30 patients with 77 tumors, owing to lack of clinical follow-up (2 patients, 6 tumors), incomplete dosimetric information (14 patients, 22 tumors), pre-existing atelectasis (9 patients, 13 tumors), atelectasis probably caused by tumor progression (5 patients, 6 tumors), and 30 tumors with negligible bronchial dose contribution (equivalent dose in 2-Gy fractions [EQD_{2,LQ}] <5 Gy₃ [$\alpha/\beta = 3$ Gy]).

Included in the analysis were 74 patients, 40 men and 34 women, treated for 108 tumors located within 2 cm from the main, lobar, or segmental bronchi; see bronchial structures in Figure 1. Of these, 46 (62%) patients were treated in Stockholm and 28 (38%) in Gothenburg. Fifty-three patients (72%) were treated for 1 tumor, 12 patients (16%) for 2 tumors, 7 patients (9%) for 3 tumors, and 2 patients (3%) for 5 tumors. All patients treated in Gothenburg had primary NSCLC, whereas patients treated in Stockholm had primary NSCLC, lung metastases, or a combination of both. The patients generally had follow-up CT scans every third month for the first year, and twice per year thereafter. All patients were followed until death, until they were lost to follow-up, or until the end of study in October 2007, when clinical examination of the patients' medical records was performed. The median time of follow-up was 18.6 months (mean, 25.9 months; range, 1.4-97.5 months). Patient characteristics are listed in Table 1.

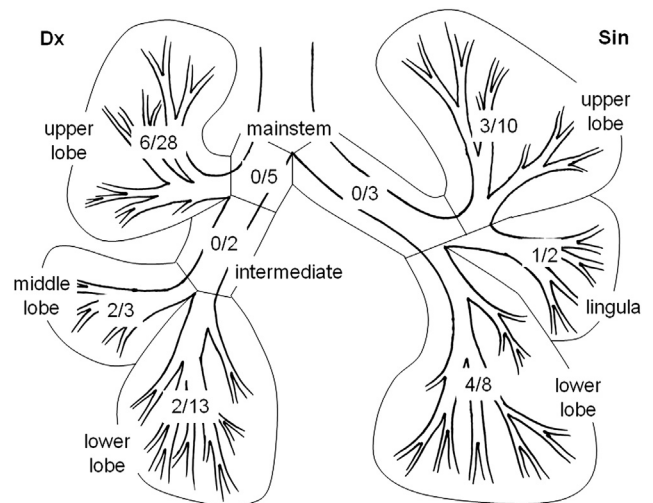


Fig. 1. Bronchial structures. Within each bronchial structure, the denominator refers to the total number of patients with high-dose regions located in that structure, and the numerator refers to the number of those patients with atelectasis.

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