

CLINICAL INVESTIGATION

Lung

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OPERABLE STAGE I
NON-SMALL-CELL LUNG CANCER: CAN SBRT BE COMPARABLE TO SURGERY?

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Purpose: To review treatment outcomes for stereotactic body radiotherapy (SBRT) in medically operable patients with Stage I non-small-cell lung cancer (NSCLC), using a Japanese multi-institutional database.

Patients and Methods: Between 1995 and 2004, a total of 87 patients with Stage I NSCLC (median age, 74 years; T1N0M0, $n = 65$; T2N0M0, $n = 22$) who were medically operable but refused surgery were treated using SBRT alone in 14 institutions. Stereotactic three-dimensional treatment was performed using noncoplanar dynamic arcs or multiple static ports. Total dose was 45–72.5 Gy at the isocenter, administered in 3–10 fractions. Median calculated biological effective dose was 116 Gy (range, 100–141 Gy). Data were collected and analyzed retrospectively.

Results: During follow-up (median, 55 months), cumulative local control rates for T1 and T2 tumors at 5 years after SBRT were 92% and 73%, respectively. Pulmonary complications above Grade 2 arose in 1 patient (1.1%). Five-year overall survival rates for Stage IA and IB subgroups were 72% and 62%, respectively. One patient who developed local recurrences safely underwent salvage surgery.

Conclusion: Stereotactic body radiotherapy is safe and promising as a radical treatment for operable Stage I NSCLC. The survival rate for SBRT is potentially comparable to that for surgery. © 2011 Elsevier Inc.

Stereotactic body radiotherapy, Lung cancer, Non-small-cell, Operable, Stage I.

INTRODUCTION

With the popularization of computed tomography (CT) screening, lung cancers are increasingly detected at an early stage. For patients with Stage I (T1 or 2, N0, M0) non-small-cell lung cancer (NSCLC), resection of the set of full lobar and systemic lymph nodes represents standard treatment. Five-year overall survival rates for clinical Stage IA and IB treated surgically are approximately 60–75% and 40–60%, respectively (1–3). However, a proportion of

patients who meet the criteria for surgery refuse such intervention for various reasons. Radiotherapy offers a therapeutic alternative in such cases, but the effects of conventional radiotherapy in patients with Stage I NSCLC are unsatisfactory, with local control rates of approximately 50% during a short 5-year survival period in 15–30% of patients (4–7). Survival rates for conventional radiotherapy for a statistically sufficient number of cases of operable Stage I NSCLC have not been reported, because most

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patients receiving radiotherapy are inoperable. The poor local control rates with conventional radiotherapy have been attributed to doses of conventional radiotherapy that are too low to control the tumor. Mehta *et al.* (8) provided a detailed theoretical analysis of NSCLC responses to radiotherapy and a rationale for dose escalation. They concluded that higher biologically effective doses (BED) irradiated during a short period must be administered to achieve successful local control of lung cancer. To provide a higher dose to the tumor without increasing adverse effects, three-dimensional conformal radiotherapy techniques have been used, and better local control and survival have recently been reported (9–11). Over the last decade, hypofractionated high-dose stereotactic body radiotherapy (SBRT) has been actively performed for early-stage lung cancer, particularly in Japan (12–17). We have previously reported preliminary results for a Japanese multi-institutional review of 257 patients with Stage I NSCLC treated with SBRT (18). The results showed that local control and survival rates were better with BED ≥ 100 Gy than with <100 Gy, and survival rates were much better for medically operable patients than for medically inoperable patients. These results were encouraging, but the duration of follow-up for the study was somewhat short (median, 38 months), and we have not presented a detailed analysis of medically operable patients as a distinct subgroup. Although the standard therapy for operable Stage I NSCLC remains surgery, the effect of SBRT on medically operable patients is an issue of great concern. We provide herein detailed and matured results of SBRT (BED ≥ 100 Gy) for medically operable patients with Stage I NSCLC, using a retrospectively collected Japanese multi-institutional database.

PATIENTS AND METHODS

Eligibility criteria

All patients who satisfied the following eligibility criteria were retrospectively collected from 14 major Japanese institutions in which SBRT for lung cancer was actively performed: (1) identification of T1N0M0 or T2N0M0 primary lung cancer on chest and abdominal CT, bronchoscopy, bone scintigraphy, or brain magnetic resonance imaging; (2) histopathologic confirmation of NSCLC; (3) medically operable cancer but selection of SBRT after refusal to undergo surgery. Medical operability was discussed within the multidisciplinary tumor board of each institution according to respiratory function, age, and complicating diseases. Basic cutoff values for medical operability were World Health Organization performance status ≤ 2 , pressure of arterial oxygen ≥ 65 mm Hg, predicted postoperative forced expiratory volume in 1 s ≥ 800 mL, no heart failure requiring pharmacotherapy, no diabetes requiring insulin, no severe arrhythmia, and no history of cardiac infarction. Positron emission tomography was not essential in the staging procedures.

Patients were informed of the concept, methodology, and rationale of this treatment, which was performed in accordance with the 1983 revision of the Declaration of Helsinki.

Table 1. Patient characteristics

Number (14 institutions)	87
Male	63
Female	24
Age (y), median (range)	74 (43–87)
ECOG performance status	
0	51
1	30
2	6
Histology	
Adenocarcinoma	54
Squamous cell carcinoma	25
Other	8
Stage	
IA	64
IB	23
Tumor diameter (mm), median (range)	25 (7–50)
IA	21
IB	39
Chronic lung disease	
Positive	38
Negative	49

Abbreviation: ECOG = Eastern Cooperative Oncology Group. Values are number unless otherwise noted.

Patient characteristics

A summary of patient pretreatment characteristics is given in Table 1. From April 1995 to March 2004, a total of 87 medically operable patients with primary NSCLC were treated using hypofractionated high-dose SBRT in 14 major Japanese institutions. Each of these 87 cases was judged medically operable, and surgery was initially recommended, but the patients declined surgery and selected SBRT as a radical treatment. Pathology of all tumors was confirmed as NSCLC by transbronchial or CT-guided percutaneous biopsy. The 14 participating institutions were these: Hokkaido University; Kyoto University; Cancer Institute Hospital; Tokyo Metropolitan Komagome Hospital; Kitasato University; Tohoku University; Hiroshima University; Tokyo Metropolitan Hiroo Hospital; Sapporo Medical University; Institute of Biomedical Research and Innovation; International Medical Center of Japan; Tenri Hospital; Kitami Red Cross Hospital; and Yamanashi University.

Treatment methods

Although the techniques to accomplish stereotactic methods differed among these institutions, all “stereotactic radiotherapy techniques” fulfilled the following five requirements: (1) reproducibility of the isocenter (setup error ≤ 5 mm), as confirmed by image guidance for every fraction; (2) respiratory motion (internal margin) suppressed using as much as possible, to <5 mm; (3) slice thickness on CT ≤ 3 mm for three-dimensional treatment planning; (4) irradiation with multiple noncoplanar static ports or dynamic arcs; and (5) single high dose ≥ 5 Gy.

Gross target volume (GTV) was delineated on CT images displayed with a lung window level. Clinical target volume (CTV) marginally exceeded GTV by 0–5 mm as judged by the individual radiation oncologist. Internal margin was

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