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Trends in stereotactic body radiation therapy for stage I small cell lung cancer

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ABSTRACT

Objectives: We aimed to report trends in stereotactic body radiation therapy (SBRT) utilization, dose prescriptions, and chemotherapy administration for stage I small cell lung cancer (SCLC) in the United States.

Materials and methods: The National Cancer Data Base (NCDB) was used to identify patients with cT1-2 N0 SCLC treated with SBRT between 2004 and 2013. Trends in SBRT use and dose prescription were analyzed over time. Multivariable logistic regression was used to determine factors associated with the administration of chemotherapy with SBRT. The Kaplan-Meier method was used to estimate overall survival.

Results: Of 9265 patients with clinical stage I SCLC who were examined for initial treatment allocation, 285 were treated with SBRT and represented the subject of the primary analysis. SBRT utilization increased from 2004 (0.4% of all stage I patients diagnosed that year) to 2013 (6.4%). During this same time period, definitive surgical management also increased from 14.9% of all patients in 2004 to 28.5% in 2013. The median SBRT biologically effective dose (BED_{10}) was 112.5 Gy (range, 72–290) and only 33 out of 285 (11.6%) received a $BED_{10} < 100$ Gy. Nearly half of all patients (130/285, 45.6%) received chemotherapy, with 42.7% of those patients receiving their chemotherapy prior to SBRT. On multivariable logistic regression, only age < 75 (the median) vs. ≥75 years (OR 4.97, 95% CI 2.96–8.35, $p < 0.001$) and year of diagnosis 2004–2008 vs. 2009–2013 (OR 2.58, 95% CI 1.27–5.26, $p = 0.009$) were predictive of chemotherapy use with SBRT. After median follow up of 45 months, the median survival was 23.5 months.

Conclusions: Our findings suggest that SBRT utilization for stage I SCLC has increased between 2004 and 2013, highlighting the need for additional research to validate the feasibility of this management approach for inoperable patients.

1. Introduction

Stereotactic body radiation therapy (SBRT) is a technique that uses stereotactic, three-dimensional targeting to facilitate the precise delivery of a short course of high dose radiation to a tumor. While its use is expanding rapidly to include several anatomical sites and malignancies, it is most widely employed as a treatment for lung tumors (including definitive treatment for stage I non-small cell lung cancer (NSCLC) patients who are either medically inoperable or who refuse surgery) [1,2]. Recent evidence suggests that SBRT for NSCLC is superior to conventionally fractionated radiotherapy (RT)[3] and may have comparable outcomes to surgical resection for those considered operable [4].

Surgical candidates with clinical stage I small cell lung cancer (SCLC) are recommended to undergo lobectomy and mediastinal lymph node dissection (after confirmatory negative pre-operative mediastinal staging) with adjuvant chemoradiation or chemotherapy depending on pathological nodal status after surgery [5]. For medically inoperable patients or those refusing surgery, National Comprehensive Cancer Network (NCCN) guidelines recommend chemotherapy with or without conventionally fractionated RT. The use of SBRT for stage I SCLC is reported only in small retrospec-

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Table 1
Patient characteristics (n = 285).

	Total Number
Age (years)	
<75	136 (47.7%)
≥75	149 (52.3%)
Gender	
Male	135 (47.4%)
Female	150 (52.6%)
Race	
White	260 (91.2%)
Other/unspecified	25 (8.8%)
Charlson-Deyo comorbidity index	
0	157 (55.1%)
≥1	128 (44.9%)
Prior cancer	
Yes	130 (45.6%)
No	155 (54.4%)
Treatment facility	
Academic	110 (38.6%)
Non-academic/unspecified	175 (61.4%)
Distance from facility	
<50 miles	245 (86.0%)
≥50 miles	32 (11.2%)
Unknown	8 (2.8%)
Median income of residential zip code	
<$46,000	110 (38.6%)
≥$46,000	174 (61.1%)
Unknown	1 (0.4%)
Patient residential county population	
<250,000	86 (30.2%)
≥250,000	199 (69.8%)
Biopsy of primary performed	
Yes	243 (85.3%)
No	42 (14.7%)
AJCC[1] Clinical T stage	
T1	232 (81.4%)
T2	53 (18.6%)
Laterality	
Right	162 (56.8%)
Left	123 (43.2%)
Biologically effective radiation dose	
<100 Gy	33 (11.6%)
≥100 Gy	252 (88.4%)
Received chemotherapy	
Yes	130 (45.6%)
No	148 (51.9%)
Unknown	7 (2.5%)

AJCC[1] = American Joint Committee on Cancer, 7th ed.

tive case series, but this modality does show promise in offering favorable treatment results for this patient cohort [6–8].

We aimed to identify trends in SBRT utilization (in the context of other possible management options), radiation dose prescriptions, and adjuvant chemotherapy administration for stage I SCLC in the United States (US) using the National Cancer Data Base (NCDB).

2. Material and methods

2.1. Data source and study cohort

We performed a retrospective study of trends in SBRT utilization for patients diagnosed with stage I (cT1-2 N0 M0) SCLC in the NCDB between 2004 and 2013. The NCDB is a national hospital-based cancer registry established by the Commission on Cancer (CoC) of the American College of Surgeons (ACS) and the American Cancer Society that serves as a comprehensive retrospective data set capturing approximately 70% of all incident cancers in the US. This data set integrates records from over 1500 CoC accredited hospitals and is de-identified (making it exempt from our Institutional Review Board). The CoC and ACS have not verified and are not responsible for the analytic or statistical methodology employed, nor for the conclusions drawn from these data by investigators.

We limited the cohort to those diagnosed with clinical stage I SCLC (9265 patients) and defined five upfront treatment approaches. Definitive SBRT was defined as radiation to the lung with biologically effective dose (BED10) of 72 to 300 Gy in fewer than 10 fractions. BED_{10} was calculated in Gray units (Gy) using the linear quadratic equation with α/β set to equal 10, d equal to the dose per fraction in Gy, and n equal to the number of fractions.

$$BED_{\alpha/\beta} = dn(1 + \frac{d}{\alpha/\beta})$$

A 10 fraction upper limit was chosen based on previously published data in NSCLC recommending more protracted fractionation regimens for large or central tumors [9]. 'Surgery' patients had surgical procedure codes 20 through 70 indicating a definitive procedure including excision or resection of less than one lobe up to and including pneumonectomy. 'Conventional external beam radiotherapy (EBRT)' was defined as radiotherapy to the lung with BED_{10} of 30–100 Gy delivered in 10–45 fractions. SBRT, surgery, and conventional EBRT patients were defined as such regardless of whether they received chemotherapy. Patients not fitting one of the above criteria but still receiving chemotherapy were assigned to the 'chemotherapy alone' cohort. Patients fitting none of the prior four criteria where placed in an 'other' category.

2.2. Statistical analysis

To identify baseline differences between SBRT patients receiving chemotherapy and those not receiving chemotherapy, chi-squared tests and multivariable logistic regression modeling were used. Patient variables were dichotomized and included age (based on median value), gender, race, Charlson/Deyo comorbidity index, prior cancer, year of diagnosis, academic vs. non-academic treatment setting, distance from treatment facility (calculated by greater circle distance), median income of residential zip code, residen-

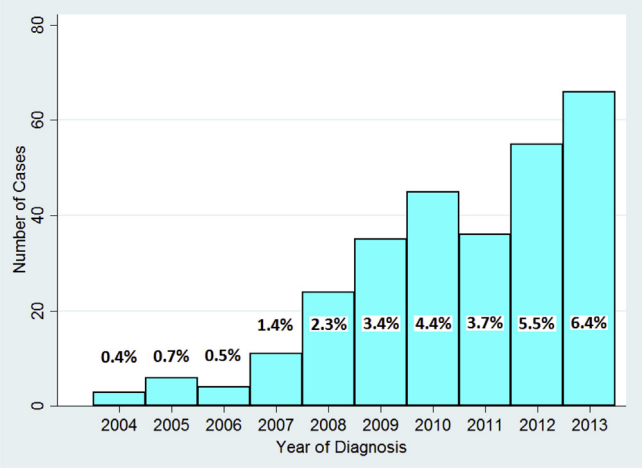

Fig. 1. National trends in stereotactic body radiation therapy (SBRT) utilization from 2004 to 2013 (n = 285).
Histogram shows number of cases on the y-axis with corresponding percentage of patients receiving SBRT out of all stage I SCLC patients diagnosed that year in the data base.