

Stereotactic Body Radiotherapy for Medically Inoperable Stage I-II Non–Small Cell Lung Cancer: The Mayo Clinic Experience

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Abstract

Objective: To examine disease control and survival after stereotactic body radiotherapy (SBRT) for medically inoperable, early-stage non–small cell lung cancer (NSCLC) and determine associations of pretreatment ^{18}F -fluorodeoxyglucose–positron emission tomography (FDG-PET) maximum standardized uptake values (SUVmax), biologically effective dose, and mediastinal staging with disease control and survival outcomes.

Patients and Methods: We retrospectively reviewed the cases of consecutive patients with FDG-PET–staged, medically inoperable NSCLC treated with SBRT at our institution between January 1, 2008, and August 4, 2014. Cumulative incidences of recurrence were estimated, accounting for the competing risk of death. Associations of SUVmax, biologically effective dose, and mediastinal staging with outcomes were evaluated using Cox proportional hazards regression models.

Results: Among 282 patients, 2-year cumulative incidences of recurrence were 4.9% (95% CI, 2.6%-8.3%) for local, 9.8% (95% CI, 6.3%-14.2%) for nodal, 10.8% (95% CI, 7.0%-15.5%) for ipsilateral lung, 6.0% (3.3%-9.8%) for contralateral lung, 9.7% (95% CI, 6.3%-14.0%) for distant recurrence, and 26.1% (95% CI, 20.4%-32.0%) for any recurrence. The 2-year overall survival was 70.4% (95% CI, 64.5%-76.8%), and the 2-year disease-free survival was 51.2% (95% CI, 44.9%-58.5%). Risk of any recurrence was significantly higher for patients with higher SUVmax (hazard ratio [per each doubling], 1.29 [95% CI, 1.05-1.59]; $P=.02$). A similar association with SUVmax was observed when considering the composite outcome of any recurrence or death (hazard ratio, 1.23 [95% CI, 1.05-1.44]; $P=.01$). The SUVmax was not significantly associated with other outcomes ($P\geq 0.69$). Two-year cumulative incidences of local recurrence for patients receiving 48 Gy in 4 fractions, 54 Gy in 3 fractions, or 50 Gy in 5 fractions were 1.7% (95% CI, 0.3%-5.6%), 3.7% (95% CI, 0.7%-11.4%), and 15.3% (95% CI, 5.9%-28.9%), respectively ($P=.02$); this difference was independent of lesion size ($P=.02$).

Conclusion: Disease control was excellent for patients who received SBRT for early-stage NSCLC, and this series represents the largest single-institution experience from the United States on SBRT for early-stage inoperable NSCLC. Higher pretreatment FDG-PET SUVmax was associated with increased risk of any recurrence, and the 50 Gy in 5 fractions dose prescription was associated with increased risk of local recurrence.

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Non–small cell lung cancer (NSCLC) is the leading cause of cancer death in the United States.¹ For patients with early-stage disease, the standard treatment recommendation is surgical resection with mediastinal lymph node dissection or

systematic sampling.² However, many patients with NSCLC have cardiac or pulmonary comorbid conditions that prevent them from being appropriate candidates for surgery. Many prospective and retrospective reports with limited follow-up have been published

regarding the efficacy of stereotactic body radiotherapy (SBRT) in providing local control (LC) in patients with both medically inoperable and operable NSCLC.³⁻⁶ In more recent series, the LC rates exceed 90%. Multiple studies have shown that delivering a higher biologically effective dose (BED) leads to better outcomes.^{7,8}

The National Comprehensive Cancer Network guidelines provide options for adjuvant therapy after surgical resection on the basis of tumor size, lymphovascular space invasion, tumor grade, and lymph node involvement.² Many patients undergoing SBRT, however, have limited tissue to evaluate these pathologic risk factors to guide adjuvant therapy decisions. Furthermore, many patients have a clinical diagnosis based solely on radiographic suspicion and patient history, given that biopsy is often considered high risk because of comorbid conditions and poor lung function. In these patients, with the limited prognostic information available other than tumor size, metabolic parameters from pretreatment positron emission tomography (PET) have been evaluated as promising prognosticators. Investigators have found mixed results, however, regarding the prognostic capability of different PET parameters: some studies have found no prognostic value,⁹⁻¹² whereas others have found that PET parameters such as maximum standardized uptake value (SUVmax), total lesion glycolysis, and metabolic tumor volume may predict disease control as well as survival.¹³⁻¹⁷

Unlike surgery, which includes pathologic lymph node assessment, SBRT does not address or treat the potential spread of malignant cells into regional lymph nodes. Therefore, regional lymph node evaluation is needed to determine whether patients are appropriate candidates for SBRT. ¹⁸F-fluorodeoxyglucose-PET (FDG-PET) has been shown to have excellent diagnostic accuracy, with a negative predictive value of 91%—an improvement compared with computed tomography (CT) alone.¹⁸ Many patients also undergo histologic evaluation of lymph nodes with mediastinoscopy or, more commonly, endobronchial ultrasonography (EBUS). This further improves the chances of accurately staging disease. It is unknown whether histologic evaluation of lymph nodes before SBRT may decrease the risk of subsequent regional failure. In one study of patients

referred for SBRT after lymph node–negative PET-CT results, 16% of patients undergoing EBUS had lymph node involvement.¹⁹ If not evaluated with EBUS, these involved nodes would have posed a risk of subsequent regional failure after treatment with SBRT alone.

In this retrospective study, we report outcomes after SBRT for patients with medically inoperable NSCLC at our institution. The primary aim was to evaluate disease control and survival outcomes after SBRT, with secondary aims of evaluating potential associations between outcomes and FDG-PET SUVmax, BED, and mediastinal staging. Toxicity associated with SBRT will be the subject of a separate future analysis.

PATIENTS AND METHODS

Study Population

Institutional review board approval was obtained for this retrospective review of consecutive patients with NSCLC treated with SBRT at 3 geographically separate campuses of our institution (designated sites 1, 2, and 3) between January 1, 2008, and August 4, 2014. Patients were included if they had American Joint Committee on Cancer clinical stage I or II, T1-T3N0M0 NSCLC, as determined by either clinical suspicion or pathologic diagnosis. Patients were excluded if they did not undergo FDG-PET staging, if they had a synchronous lung cancer lesion, prior lung cancer, history of other cancer that was possibly presenting as a lung metastasis, or if they did not have any follow-up after SBRT treatment.

All patients underwent pretreatment PET. Patients were required to have follow-up chest CT, most often performed every 3 months. Measured outcomes included local recurrence, nodal recurrence, ipsilateral lung recurrence, contralateral lung recurrence, distant recurrence, any recurrence, disease-free survival (DFS), and overall survival (OS). The baseline time point for all outcomes was the day of the first SBRT treatment.

Radiation Treatment

Patients were treated with target definitions and treatment planning consistent with Radiation Therapy Oncology Group (RTOG) protocols.²⁰⁻²³ In most cases, a gross tumor volume was created based on lung windows from

TABLE 1. Patient and Treatment Characteristics^{a,b}

Characteristic	Value (N=282)
Age (y)	76 (51-94)
Men	130 (46.1)
Lesion size (cm)	2.1 (0.6-6.6)
Institution location	
Site 1	152 (53.9)
Site 2	69 (24.5)
Site 3	61 (21.6)
SUVmax T category	6.5 (0.6-38.4)
1a	132 (46.8)
1b	88 (31.2)
2a	54 (19.1)
3	8 (2.8)
Biopsy of primary lesion	196 (69.5)
Histologic diagnosis (N=196)	
Adenocarcinoma	99 (50.5)
Squamous cell carcinoma	70 (35.7)
NOS	27 (13.8)
Mediastinal staging	90 (31.9)
BED (Gy/fractions)	
48/4	148 (52.5)
54/3	67 (23.8)
50/5	56 (19.9)
57.5/5	3 (1.1)
60/5	2 (0.7)
45/5	1 (0.4)
50/4	1 (0.4)
54/5	1 (0.4)
55/5	1 (0.4)
56/4	1 (0.4)
60/3	1 (0.4)

^aBED = biologically effective dose; NOS = not otherwise specified; SUVmax = maximum standardized uptake value.

^bData are presented as median (range) or No. (percentage) of patients. Percentages may not total 100 because of rounding.

planning CT. Four-dimensional CT was obtained at the time of CT simulation to create an internal target volume (ITV). A uniform 5-mm planning target volume expansion was typically performed after ITV creation. If no ITV was available, the planning target volume expansion was 5 mm axially and 1 cm in the superior and inferior dimensions. Prescription doses ranged from 48 to 60 Gy in 3 to 5 fractions (shown as Gy/fractions). Dose constraints for organs at risk were also extrapolated from RTOG protocols.

Statistical Analyses

The cumulative incidences of local recurrence, nodal recurrence, ipsilateral lung recurrence, contralateral lung recurrence, distant recurrence,

and any recurrence were estimated while accounting for the competing risk of death.²⁴ Overall survival and DFS were estimated using the Kaplan-Meier method. Censoring occurred at the date of last follow-up.

For evaluation of the association between FDG-PET SUVmax and outcomes, unadjusted Cox proportional hazards regression models were used, in which SUVmax was examined on a logarithmic scale owing to its skewed distribution. Hazard ratios (HRs) and 95% CIs were estimated, and the cause-specific hazard of the given outcome was modeled.²⁵ The associations between BED and local recurrence and between mediastinal staging and nodal recurrence were also examined using unadjusted Cox regression models. For the association between BED and local recurrence, we also examined the sensitivity of our Cox regression results to the adjustment for lesion size. $P < .05$ was considered statistically significant in all analyses, and all statistical tests were 2-sided. Statistical analyses were performed using SAS software, version 9.2 (SAS Institute) and R statistical software, version 3.1.1 (R Foundation for Statistical Computing).

RESULTS

Review of patient databases identified a total of 282 patients for inclusion at the 3 sites—152 at site 1, 69 at site 2, and 61 at site 3. Patient and treatment characteristics are presented in [Table 1](#). The median age was 76 years (range, 51-94 years), and 130 patients (46.1%) were men. The median tumor size was 2.1 cm, and median FDG-PET SUVmax was 6.5. Most patients had either T1a (132 [46.8%]), T1b (88 [31.2%]), or T2a (54 [19.1%]) lesions. Among the 196 patients (69.5%) who underwent biopsy, most lesions (99 [50.5%]) were diagnosed as adenocarcinoma, 70 (35.7%) were squamous cell carcinoma, and 27 (13.8%) were not otherwise specified. Of the 282 patients, 90 (31.9%) underwent mediastinal lymph node evaluation before treatment, mostly with EBUS. The median duration of follow-up after the first SBRT treatment was 20.4 months (range, 2.5-76.6 months).

Summary of Clinical Outcomes

A summary of clinical outcomes is provided in [Table 2](#). A total of 79 patients (28.0%) had disease recurrence of any type, which corresponds to a 2-year cumulative incidence of 26.1%

(95% CI, 20.4%-32.0%). The most common type of specific recurrence was ipsilateral lung recurrence, with a 2-year cumulative incidence of 10.8% (95% CI, 7.0%-15.5%), followed by nodal recurrence (9.8%; 95% CI, 6.3%-14.2%), distant recurrence (9.7%; 95% CI, 6.3%-14.0%), contralateral lung recurrence (6.0%; 95% CI, 3.3%-9.8%), and local recurrence (4.9%; 95% CI, 2.6%-8.3%). A total of 110 patients (39.0%) died during follow-up; OS was 90.3% (95% CI, 86.8%-94.0%) at 1 year and 70.4% (95% CI, 64.5%-76.8%) at 2 years. The 1-year and 2-year DFS estimates were 89.8% (95% CI, 86.2%-93.4%) and 51.2% (95% CI, 44.9%-58.5%), respectively.

Association Between SUVmax and Outcomes

Associations between SUVmax and clinical outcomes are shown in Table 3. There was evidence of an association between a higher SUVmax and an increased risk of any recurrence (HR, 1.29; 95% CI, 1.05-1.59; $P=.02$). This association is further illustrated in Figure 1, in which SUVmax was divided into 3 categories (low, moderate, or high) by approximate sample tertiles. A similar significant association with SUVmax was observed for the composite outcome of any recurrence or death (HR, 1.23; 95% CI, 1.05-1.44; $P=.01$). Maximum standardized uptake value was not significantly associated with the more specific outcomes of local recurrence, nodal recurrence, ipsilateral lung recurrence, contralateral lung recurrence, distant recurrence, or death (Table 3).

Association Between BED and Local Recurrence

Among the 282 study patients, the 3 most common dose prescriptions were 48/4 (n=148; 52.5%), 54/3 (n=67; 23.8%), and 50/5 (n=56; 19.9%). Two-year local recurrence rates by BED for patients receiving 48/4, 54/3, and 50/5 were 1.7%, 3.7%, and 15.3%, respectively ($P=.02$) (Figure 2). Specifically, compared with the most common group (48/4), the risk of local recurrence was not significantly higher for the 54/3 group (HR, 2.36; 95% CI, 0.23-5.69; $P=.68$) but was significantly higher for the 50/5 group (HR, 5.88; 95% CI, 1.72-20.05; $P=.005$). On further examination, lesion size was

TABLE 2. Summary of Outcomes (N=282)

Outcome	No. (%) of patients	Cumulative incidence (95% CI) after SBRT (%)	
		12 months	24 months
Local recurrence	15 (5.3)	2.0 (0.7-4.3)	4.9 (2.6-8.3)
Nodal recurrence	32 (11.3)	5.1 (2.9-8.3)	9.8 (6.3-14.2)
Ipsilateral lung recurrence	33 (11.7)	4.0 (2.0-6.9)	10.8 (7.0-15.5)
Contralateral lung recurrence	23 (8.2)	2.4 (1.0-4.8)	6.0 (3.3-9.8)
Distant recurrence	29 (10.3)	7.0 (4.3-10.6)	9.7 (6.3-14.0)
Any recurrence	79 (28.0)	14.4 (10.4-19.0)	26.1 (20.4-32.0)
Any recurrence or death	141 (50.0)	10.2 (6.6-13.8)	48.8 (41.5-55.1)
Death	110 (39.0)	9.7 (6.0-13.2)	29.6 (23.2-35.5)

SBRT = stereotactic body radiotherapy.

significantly different between the 3 BED groups; median lesion size for the 48/4, 54/3, and 50/5 groups were 2.2 cm, 1.8 cm, and 2.5 cm, respectively ($P<.001$). However, when adjusting for lesion size in a multivariate Cox regression model, the aforementioned difference in local recurrence between patients receiving 48/4, 54/3, and 50/5 remained significant ($P=.02$), which indicates that this difference was independent of lesion size.

Association Between Mediastinal Staging and Nodal Recurrence

Mediastinal staging was not significantly associated with risk of nodal recurrence (HR, 1.42;

TABLE 3. Association Between SUVmax and Various Outcomes^{a,b}

Outcome	HR (95% CI) ^c	P value
Local recurrence	0.91 (0.57-1.45)	.69
Nodal recurrence	0.96 (0.70-1.32)	.79
Ipsilateral lung recurrence	0.97 (0.71-1.33)	.84
Contralateral lung recurrence	1.04 (0.71-1.52)	.85
Distant recurrence	1.02 (0.73-1.44)	.89
Any recurrence	1.29 (1.05-1.59)	.02
Any recurrence or death	1.23 (1.05-1.44)	.01
Death	1.01 (0.85-1.20)	.89

^aHR = hazard ratio; SUVmax = maximum standardized uptake value.

^bHRs, 95% CIs, and P values result from unadjusted Cox proportional hazards models, in which the cause-specific hazard of the given outcome was modeled.

^cHRs for each doubling of SUVmax, which was examined on the logarithmic scale in Cox regression analysis because of skewed distribution.

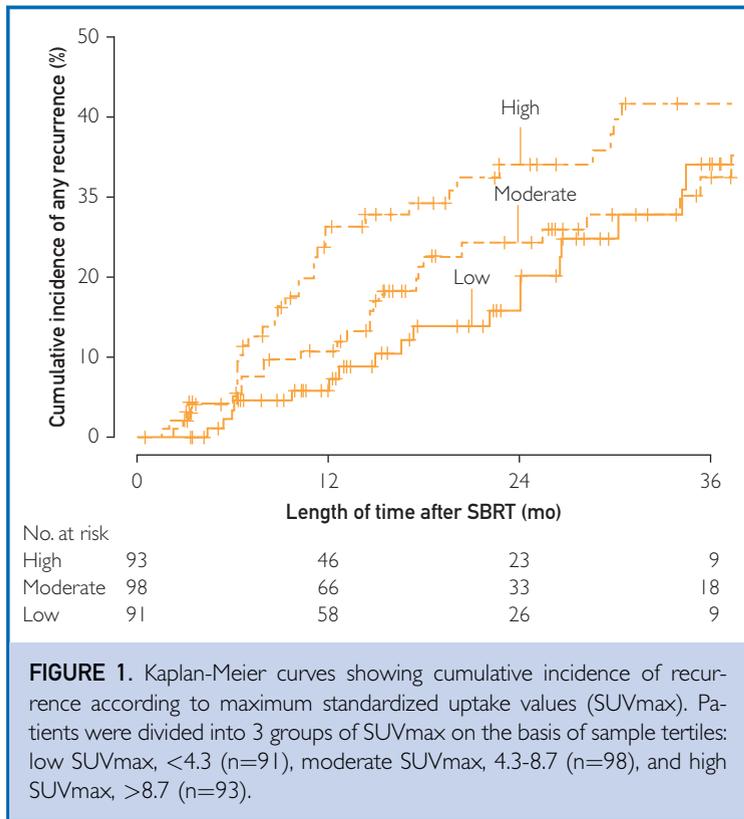


FIGURE 1. Kaplan-Meier curves showing cumulative incidence of recurrence according to maximum standardized uptake values (SUVmax). Patients were divided into 3 groups of SUVmax on the basis of sample tertiles: low SUVmax, <4.3 (n=91), moderate SUVmax, 4.3-8.7 (n=98), and high SUVmax, >8.7 (n=93).

95% CI, 0.68-2.94; $P=.35$); cumulative 2-year incidences in patients with and without mediastinal staging were 11.8% (95% CI, 5.3%-21.2%) and 8.9% (95% CI, 5.0%-14.0%), respectively. Of note, however, the rates of mediastinal evaluation at sites 1 and 2 were 23.0% (35 of 152 patients) and 11.6% (8 of 69 patients), respectively, much lower than at site 3, where mediastinal evaluation was routinely performed (77.0% [47 of 61 patients]). Thus, selection bias may be present for patients undergoing mediastinal evaluation. At site 3, where EBUS was more consistently performed, the crude rates of nodal failure for patients with and without preliminary EBUS were 12.8% and 21.4%, respectively, although the difference was not statistically significant (HR, 0.82; 95% CI, 0.20-3.33; $P=.78$).

DISCUSSION

We report excellent disease control in this large series of patients who received SBRT for early-stage NSCLC. To our knowledge, our study represents the largest single-institution experience from the United States on SBRT for early-stage

inoperable NSCLC. The 2-year LC of 95.1% is consistent with the results of other retrospective studies, which have shown 2-year LC rates ranging from 64% to 95% (Table 4).^{3,4,6,26-37} One limitation of our outcome data is that not all patients underwent biopsy before radiation (69.5% biopsy rate). However, in other studies reporting outcomes of patients treated with or without biopsy, LC, distant metastasis, and OS appear similar between the groups.³⁸ In the literature on retrospective studies, the biopsy rate ranges from 35% to 100% (Table 4). Examining the prospective data, in which most trials have required a biopsy, the 3-year LC rate ranges from 84% to 98% (Table 4). Thus, SBRT appears to result in better LC than conventional external beam radiotherapy, which has LC rates of approximately 70% for stage I NSCLC.³⁹ In terms of regional control, the 2-year nodal failure rate of 10% in our study is consistent with other retrospective and prospective data showing 4% to 13% nodal failure rates (Table 4). Others have shown low rates of nodal failure despite patients having only clinical staging. For example, in a retrospective study of 676 patients who underwent SBRT, Senthil et al⁶ reported a 2-year regional control rate of 92% for patients with clinical stage I and II NSCLC.

Rates of distant metastasis have varied among studies, partly because of the definition of distant metastasis. In the current study, we elected to separate contralateral lung nodules from other distant organ failures. Our combined rate of contralateral lung failures (6.0%) and other distant failures (9.7%) would be consistent with the failure rates seen in prospective studies.⁴

The value of pretreatment FDG-PET in predicting outcomes for inoperable NSCLC treated with SBRT is controversial. The available studies report conflicting results. Several series showed that PET results are not prognostic for various outcomes such as local failure, regional failure, distant metastasis, DFS, or OS. Burdick et al¹¹ analyzed 72 patients with medically inoperable T1-T2N0M0 NSCLC treated with SBRT and concluded that pretreatment PET SUVmax did not predict LC, regional failure, distant metastasis, or OS. Similarly, Hoopes et al¹⁰ reviewed 58 cases of inoperable, clinical stage I NSCLC in prospective phase I and II trials of SBRT and did not find pre-SBRT PET SUVmax to be a

predictor of LC or OS. Many factors may contribute to the lack of association between PET data and prognosis. For example, the particular PET findings that should be evaluated—whether SUVmax, retention index, metabolic tumor volume, total lesion glycolysis, or some other parameter—have not been agreed upon. Most series have few patients and may not have enough events to show statistical significance for local or regional control. Also, other factors may influence the measurement of SUVmax, including duration of fasting time before PET and spatial resolution.

In contrast, multiple studies have shown that SUVmax is prognostic for tumor recurrence.¹³⁻¹⁷ Clarke et al¹⁴ showed that SUVmax greater than 5 was the most significant cutoff point for predicting distant metastasis ($P=.01$). Among 152 patients with T1-T2N0M0 NSCLC treated with SBRT, Takeda et al¹⁵ found that an SUVmax greater than 2.47 predicted worse 3-year DFS (58.3% vs 93%; $P<.001$) and that an SUVmax greater than 2.55 predicted worse 3-year OS (42.2% vs 86.5%; $P<.001$). In the current study, patients with a higher SUVmax were more likely to experience any recurrence compared with patients with a lower SUVmax. The overall number of events in our study may be too few to demonstrate an association of SUVmax with any single particular outcome, such as LC, but these events as an aggregate did allow for association to be demonstrated. Further prospective studies are needed to determine whether additional treatment in this higher-risk cohort may decrease the risk of recurrence and improve outcomes. However, many of these patients have underlying comorbid conditions, and any additional therapy would need to be weighed against possible increases in treatment toxicity in this patient population.

Patients treated with higher BED regimens (54/3 or 48/4) had better LC than patients treated with 50/5, and this finding was independent of lesion size. Other studies have previously demonstrated that delivering a higher BED can improve outcomes.^{7,8} However, the ideal dose regimen for optimizing LC and minimizing toxicities continues to be a subject of investigation. The RTOG 0813 study is a closed phase 1-2 dose escalation trial that will help determine the optimal SBRT dose for medically inoperable, centrally located tumors. The starting dose in this trial was 50/5 and was escalated

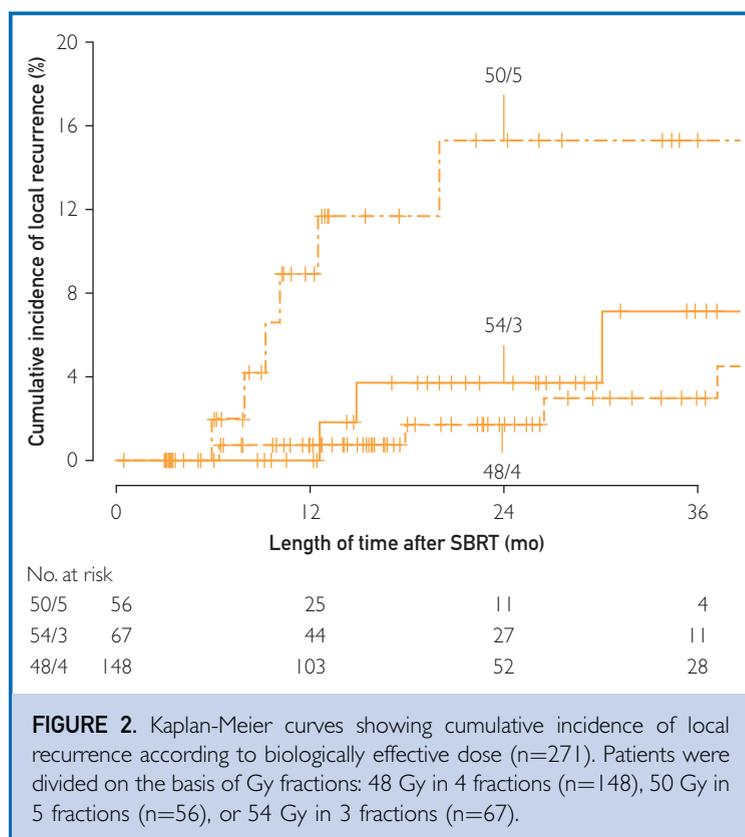


FIGURE 2. Kaplan-Meier curves showing cumulative incidence of local recurrence according to biologically effective dose ($n=271$). Patients were divided on the basis of Gy fractions: 48 Gy in 4 fractions ($n=148$), 50 Gy in 5 fractions ($n=56$), or 54 Gy in 3 fractions ($n=67$).

by 2.5 Gy to a maximum dose of 60/5, with maximum tolerated dose and treatment efficacy being the primary end points. Early results presented at the American Society for Radiation Oncology 2015 annual meeting regarding toxicity with a median follow-up of 26.6 months showed a maximum tolerated dose of 60/5 with a 7.2% risk of dose-limiting toxicity.⁴⁰ The phase 2 efficacy component of the study will help determine the optimal dose for central lesions. Given our finding of inferior LC with 50/5, it is possible that one of the higher doses used in RTOG 0813 may be optimal for central lesions.

For peripheral lesions, RTOG 0915 is a closed phase 2 trial that compared 48/4 vs 34/1 in patients with medically inoperable NSCLC; the authors concluded that 34/1 should be further researched in future SBRT trials.⁵ We found LC to be greater than 95% for patients receiving either 48/4 or 54/3. Our study group did not include any patients with single-fraction treatment, so further research will assist in identifying the ideal dose for peripheral lesions.

TABLE 4. Comparison of Selected Retrospective and Prospective SBRT Studies

Reference, year	Tumor size (cm)							
	No.	Med	Max	Bx proven (%)	FU (mo)	LC (%)	Nodal failure (%)	OS (%)
Retrospective series								
Onimaru et al, ²⁶ 2008	28	NA	NA	NA	27	64	NA	NA
Stephans et al, ²⁷ 2009	94	2.3	6	65	15	95	9	75
Crabtree et al, ²⁸ 2010	76	NA	NA	80	19	89	4	32
Haasbeek et al, ²⁹ 2011	63	3.6	7.4	38	35	93	9	69
Matsuo et al, ³⁰ 2012	66	NA	NA	100	36	NA	NA	45
Senthi et al, ⁶ 2012	676	2.7	10.7	35	33	95	8	60
Grills et al, ³¹ 2012	505	2.6	8.5	64	19	94	11	60
Current series	282	2.1	6.6	70	20	95	10	70
Prospective series								
Timmerman et al, ³² 2006	70	3.1	7	100	18	95	NA	55
Zimmermann et al, ³³ 2006	68	NA	NA	100	17	88	6	53
Fakiris et al, ³ 2009	70	NA	7	100	50	88	9	43
Baumann et al, ³⁴ 2009	57	2.5	5	67	35	92	5	65
Timmerman et al, ⁴ 2010	55	NA	5	100	34	98	4	56
Ricardi et al, ³⁵ 2010	62	2.4	5	65	28	88	13	69
Bral et al, ³⁶ 2011	40	2.8	6	100	16	84	5	52
Nagata et al, ³⁷ 2015	100	2.1	3	100	47	85	8	60

Bx = biopsy; FU = follow-up; LC = local control; Max = maximum; Med = median; NA = not available; OS = overall survival; SBRT = stereotactic body radiotherapy.

This study has limitations inherent to retrospective studies. Although treatment was planned based on RTOG protocol guidelines, there was no independent review of treatment plans to ensure that there were no deviations from these guidelines. Selection bias may have occurred in patients who underwent EBUS among the 3 treatment sites, which limits our analysis regarding whether EBUS staging can help decrease nodal failures after SBRT. Follow-up was typically performed with chest CT every 3 months after completion of treatment, but because this was not a prospective protocol, actual follow-up schedule and studies may have varied between patients.

CONCLUSION

Our analysis of a large cohort of patients with NSCLC confirms the reproducibility of SBRT in multiple smaller trials and helps strengthen the evidence supporting SBRT as an excellent treatment option for medically inoperable early-stage lung cancer. We found that higher pretreatment FDG-PET SUVmax was associated with increased risk of any recurrence, and the 50 Gy in 5 fraction prescription was associated with increased risk of local recurrence.

Abbreviations and Acronyms: BED = biologically effective dose; CT = computed tomography; DFS = disease-free survival; EBUS = endobronchial ultrasonography; FDG-PET = ¹⁸F-fluorodeoxyglucose-positron emission tomography; HR = hazard ratio; ITV = internal target volume; LC = local control; NSCLC = non-small cell lung cancer; OS = overall survival; PET = positron emission tomography; RTOG = Radiation Therapy Oncology Group; SBRT = stereotactic body radiotherapy; SUVmax = maximum standardized uptake value

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