Size matters: A comparison of T1 and T2 peripheral non–small-cell lung cancers treated with stereotactic body radiation therapy (SBRT)

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Objective: The purpose of this study was to compare the outcomes and local control rates of patients with peripheral T1 and T2 non–small-cell lung cancer treated with stereotactic body radiation therapy.

Methods: The records of 40 consecutive patients treated with 3- or 5-fraction lung stereotactic body radiation therapy for peripheral, clinical stage I non–small-cell lung cancer were reviewed. Stereotactic body radiation therapy was delivered at a median dose of 60 Gy. Doses to organs at risk were limited based on the Radiation Therapy Oncology Group 0236 treatment protocol. Patients were staged clinically. Median follow was 12.5 months.

Results: Twenty-seven (67%) patients and 13 (33%) patients had T1 and T2 tumors, respectively. Thirty-seven (94%) patients were medically inoperable. Nine (23%) patients had chest wall pain after stereotactic body radiation therapy. Symptomatic pneumonitis developed in 4 (10%) patients. Increasing tumor size correlated with worse local control and overall survival. The median recurrence-free survival for T1 and T2 tumors was 30.6 months (95% confidence interval [CI], 26.9–34.2) and 20.5 months (95% CI, 14.3–26.5), respectively ($P = .038$). Local control at 2 years was 90% and 70% in T1 and T2 tumors, respectively ($P = .03$). The median survival for T1 and T2 tumors was 20 months (95% CI, 20.1–31.6) and 16.7 months (95% CI, 10.8–21.2), respectively ($P = .073$).

Conclusions: Stereotactic body radiation therapy for T2 non–small-cell lung cancer has a higher local recurrence rate and trended toward a worse survival than did T1 lesions. Tumor size is an important predictor of response to stereotactic body radiation therapy and should be considered in treatment planning. (*J Thorac Cardiovasc Surg* 2010;140:583-9)

INTRODUCTION

Early-stage (T1-2 N0) primary non–small-cell lung cancer (NSCLC) traditionally has been managed with surgical resection. Anatomic surgical resection, usually with a lobectomy, for these early-stage tumors has resulted in 3- to 5-year survivals of 60% to 80%.^{1,2} Unfortunately, significant complications are associated with lobectomy in elderly patients or those with medical comorbidities such as poor pulmonary reserve or cardiovascular disease.^{3,4} More limited surgical procedures (wedge resection or segmentectomy) may be used but are associated with poorer outcomes than are definitive surgical procedures.⁵ Historically, external beam radiation therapy has been used as a primary treatment modality for patients with early-stage NSCLC who are not operative candidates. This standard 3-dimensional conformal therapy approach uses small daily fractions of radiation of 1.8 to 2 Gy for a total

dose of 50 to 66 Gy. Suboptimal 5-year survivals of 10% to 30% (median survival, 12–16 months) and 5-year local control rates of 50% to 70% have been reported with this technique.^{6,7}

The recognition that dose escalation is an important component for improved tumor control led to the development of stereotactic body radiation therapy (SBRT). SBRT uses elements of 3-dimensional conformal therapy combined with stereotactic tumor localization to deliver significantly higher daily doses of radiation while limiting radiation dose to the surrounding normal tissues. Results from North America and Europe have shown 3-year local control rates of 70% to 90% with 2-year survivals of approximately 50%.⁸⁻¹⁰ Intuitively, tumor size would be expected to be an independent predictor of local failure. Prior prospective studies using lung SBRT failed to show any difference in local control or median survival based on tumor T staging.¹¹ The purpose of this study was to determine how tumor T stage affects the overall survival and local control rates in patients treated with lung SBRT for early-stage NSCLC.

METHODS

Patient Eligibility and Characteristics

Between March 2005 and January 2008, 60 patients with primary NSCLC were treated with SBRT at the University of Virginia after institutional review board approval for an institutional protocol. Forty patients

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Abbreviations and Acronyms

BED	= biologic equivalent dose
CI	= confidence interval
CT	= computed tomography
FDG	= fluorodeoxyglucose
GTV	= gross tumor volume
HR	= hazard ratio
NSCLC	= non-small-cell lung cancer
PET	= positron emission tomography
PTV	= planning target volume
SBRT	= stereotactic body radiation therapy
SUV	= standardized uptake value
V20	= volume of lung receiving 20 Gy

with peripheral primary NSCLC were identified and reviewed. Peripheral tumors were defined by the Radiation Therapy Oncology Group protocols as the primary tumor not touching a volume 2 cm in all directions around the proximal bronchial tree (distal 2 cm of the trachea, main stem bronchi, and lobar bronchi). The median patient age was 73 years (range, 54–87 years). All patients were required to undergo computed tomography (CT) of the chest and abdomen for clinical staging. No patients in our cohort underwent mediastinoscopy or endobronchial ultrasound owing to medical comorbidities. On the basis of CT imaging, patients were classified as having clinical stage I (T1-2 N0) according to the American Joint Committee on Cancer staging. Positron emission tomography (PET)-CT scans were obtained as part of the initial staging workup in 34 (85%) patients. Histologic confirmation of cancer was obtained in all patients by either tissue biopsy or cytology. Patients with abnormal fluorodeoxyglucose (FDG) uptake (maximum standardized uptake value [SUV] > 2.5) in the mediastinum were not considered candidates for SBRT.

All patients were evaluated by a thoracic surgeon and radiation oncologist at our institution. Patients were treated with lung SBRT if they were considered to be in medically inoperable condition or if they refused surgery. Patients were considered to be medically inoperable owing to an underlying physiologic condition prohibiting a potentially curable resection based on a low probability of tolerating anesthesia, the operation, or the recovery period. Guidelines for inoperability were determined by the thoracic surgeon and typically included a predicted postoperative forced expiratory volume in 1 second of less than 30%, severely reduced diffusion capacity greater 40% predicted, a performance status of 3 or greater, or severe cardiac disease. No patients received prior lung irradiation.

Pretreatment Assessment and Follow-up

Before SBRT was initiated, all patients underwent the following evaluation: physical examination, weight and performance status assessment, pulmonary function tests, and CT scan of the chest. After SBRT, follow-up was performed approximately 4 to 8 weeks after treatment and approximately every 3 months thereafter. CT of the chest was routinely obtained at 3-month intervals from the completion of radiotherapy. PET-CT was not routinely obtained before the initiation of therapy. Twelve patients underwent pretreatment and posttreatment PET-CT scans. The median time from the end of treatment until PET-CT acquisition was 9.8 months. Tumor response was defined as a decrease in the maximum tumor diameter by 30% on CT imaging or decrease in abnormal FDG uptake of the tumor by 20% as measured by maximum SUV. Local tumor recurrence was defined as a 20% increase in the largest tumor diameter on successive follow-up imaging at 3-month intervals based on Response Evaluation Criteria in Solid Tumors (RECIST).¹² Lobar recurrences were defined as local recurrences. Local re-

currence as demonstrated by an increase in abnormal FDG uptake was required to correspond to an enlarging CT abnormality. Metastatic recurrence was defined as both regional nodal recurrence (N1 or N2) and distant systemic metastases. Distant recurrence was determined by imaging (CT or PET) and not confirmed pathologically unless amenable to percutaneous biopsy. Toxicity was graded using the Common Toxicity Criteria for Adverse Events (CTCAE v3.0).

SBRT Planning

All patients underwent treatment planning scans using free breathing helical CT imaging. Patients were immobilized using a “frameless” semirigid evacuated bag system (Vac-Lok; MEDTEC, Orange City, Iowa). An isocenter was placed in the geometric center of the tumor. Isocenter coordinates were used for daily alignment for subsequent treatments. The gross tumor volume (GTV) was identified on each axial CT slice using pulmonary windowing. Solid components and adjacent ground-glass opacity were included in the volume. The clinical target volume was identical to the GTV. In patients who underwent pretreatment PET-CT scans, PET imaging was not used for treatment planning purposes. The planning target volume (PTV) was intended to account for setup variability and target motion. The volume was designed by expanding the GTV 0.5 cm in the radial direction and 1.0 cm in the cranial-caudal direction to account for tumor motion during a normal respiratory cycle as determined by the Radiation Therapy Oncology Group 0236 protocol. Normal tissue dose constraints were as follows: for the heart, trachea, and ipsilateral bronchus, a 30-Gy maximum point dose; for the esophagus, a 27-Gy maximum point dose; for the brachial plexus, a 24-Gy maximum point dose; and for the spinal cord, an 18-Gy maximum point dose.

Treatment planning was coordinated with both the thoracic surgeons and the radiation oncologists and performed using Hi-Art Helical TomoTherapy inverse planning software (Tomotherapy, Madison, Wis). Lung and bone density corrections were used for planning. The dose was prescribed such that 100% of the dose covered 95% of the PTV. The median prescribed dose in our cohort was 60 Gy (range, 42–60 Gy) in 3 to 5 fractions. The median biologic equivalent dose (BED) for the cohort was 150 Gy (range, 78–180 Gy). The selection of total doses and fractionation to the primary tumor was determined by constraints to the adjacent normal tissues. Figure 1 shows a typical SBRT treatment plan. The prescribed dose was not dictated by T stage or tumor size. Successful planning attempted to meet the following criteria: (1) conformity of the PTV as judged by the volume of the prescription isodose to the PTV should be less than 1.2 with minor deviations occurring 1.2 to 1.4; (2) any dose greater than 105% of the prescription should fall within the PTV; (3) heterogeneity of the PTV as judged by the dose to 5% of the PTV to the dose to 95% of the PTV should be less than 1.2; (4) volume of lung receiving 20 Gy should be less than 10% (V20).

Statistical Analysis

The follow-up was determined from the date of the final SBRT treatment to calculate median follow-up and Kaplan-Meier outcome data including local control and overall survival. SPSS (SPSS, Inc, Chicago, Ill) was used for statistical analysis. Log-rank tests were used to compare outcome data between T-stage groups. A Cox regression analysis was performed to adjust outcomes based on patient-specific data using multiple variables analyzed simultaneously.

RESULTS

The patient and tumor characteristics are listed in Table 1. The most common reason for inoperability was poor pulmonary reserve, which was identified in 26 patients (median forced expiratory volume in 1 second 33% of predicted, median diffusion capacity 30% of predicted). Other reasons

FIGURE 1. Representative helical TomoTherapy SBRT treatment plan with isodose lines and corresponding BED.

that patients were deemed to be in inoperable condition included severe coronary artery disease not amenable to revascularization (3 patients) or cardiac dysfunction with an ejection fraction less than 30% (5 patients) and a Karnofsky performance status less than 70% (3 patients). Seventy percent of patients were dependent on supplemental oxygen. Three (8%) patients refused surgical management of their disease including mediastinal staging with endobronchial ultrasound or mediastinoscopy. All patients completed intended radiotherapy without interruption. The median follow-up time for the entire cohort from the end of treatment was 12.5 months (range, 2–35 months). There was

TABLE 1. Patient and tumor characteristics

Median age (y)	73 (54–87)
Median tumor diameter (cm)	2.3 (0.9–6.5)
Tumor stage	
T1	27
T2	13
Median follow-up (mo)	12.5 (2.1–34.7)
T1	14.5 (3–34.7)
T2	11.2 (2.1–26)
	<i>P</i> = .25
Median total dose (Gy)	60 (42.5–60)
T1	60 (42.5–60)
T2	55 (45–60)
	<i>P</i> = .13
Median BED (Gy)	150 (78–180)
T1	150 (78.6–180)
T2	150 (85.5–180)
	<i>P</i> = .07

BED, Biologic equivalent dose.

no statistical difference in follow-up, nominal radiation dose, or BED between the patients with T1 and T2 tumors (see Table 1).

The median tumor size was 23 mm (range, 9–50 mm) with 27 (67%) and 13 (33%) having T1 and T2 tumors, respectively. All tumors were peripheral in the lung. The median distance to the chest wall was 4 mm (range, 0–25 mm). Twenty-six patients had primary tumors located in the upper lobe of the lungs, 12 in the lower lobe, and 2 in the right middle lobe.

The median PTV was 39.8 mL (range, 7.98–47.0 mL) for T1 tumors and 103 mL (range 40.5–196 mL) for T2 tumors. Thirty-two (80%) patients meet plan criteria for conformality with an index less than 1.2. Eight (20%) patients were considered to have minor deviations (conformality index 1.2–1.4). The mean conformality index was 1.17 (SD ± 0.12). All plans met the criteria for heterogeneity with a mean heterogeneity index of 1.06 (SD ± 0.04). The mean V20 for the cohort was 8.08% (SD ± 3.4%). The median beam-on time per fraction was 22 minutes.

Toxicity data are listed in Table 2. Twenty-three percent of patients (9/40) had chest wall pain. The median time to onset of chest wall pain was 7.1 months (range, 0.6–32.3 months). The median time to resolution of chest wall pain was 4.6 months (range, 0.7–10.5 months). Two (5%) patients were identified as having a rib fracture as documented by chest CT. The median time to diagnosis of rib fracture was 20.6 months (range, 8.9–33.3 months). Symptomatic pulmonary complications (>grade 1) occurred in approximately 10% of patients, with 1 patient having grade 3 and grade 4 pneumonitis. No treatment-related deaths occurred.

TABLE 2. Toxicity data

	No. (n = 40)
Chest wall pain	9 (23%)
Rib fracture	2 (5%)
Pneumonitis	2
Grade 1	5 (12%)
Grade 2	1 (2%)
Grade 3	1 (2%)
	Median (range)
Onset of pain (mo)	7.1 (0.6–32.3)
Time to rib fracture (mo)	20.6 (8.9–33.3)

Of the 12 patients who underwent pretreatment and posttreatment PET-CT imaging, the median pretreatment maximum SUV was 6.0 (range, 1.0–16.2). Sixty-six percent (8/12) had a decrease in their 9-month posttreatment maximum SUV with a median value of 2.0 (range, 0–10.9). The mean maximum SUV reduction was 56% (range, 18%–100%). Thirty-four percent of patients (4/12) had an increase in their tumor posttreatment maximum SUV with a mean increase of 38% (range, 24%–60%).

Seven (17%) patients had local tumor recurrence with or without distant recurrence. Eight patients (stage T1 = 5, stage T2 = 3) had distant recurrence, 2 of whom had documented local recurrence at the time of distant metastatic disease. Overall survival and local control (Figures 2 and 3) were determined for the entire cohort. The overall local control at 2 years for the entire cohort was 83%. The

mean recurrence-free survival for the entire cohort was 27.1 months (95% confidence interval [CI], 22.6–31.6). Differences in local control were evaluated on the basis of tumor size and clinical T stage. Increasing size correlated with increased local failure (hazard ratio [HR], 1.904; 95% CI, 1.130–3.210; $P = .016$). Local control at 2 years for T1 tumors was 90%, whereas local control was 70% for T2 tumors ($P = .035$). The median recurrence-free survival for T1 and T2 tumors was 30.6 months (95% CI, 26.9–34.2) and 20.5 months (95% CI, 14.3–26.5), respectively ($P = .038$). The mean time to local recurrence for T1 and T2 tumors was 16 and 7.5 months, respectively. Local control for both T-stage groups was independent of patient age (HR, 1.074; 95% CI, 0.950–1.214), tumor histology (HR, 0.466; 95% CI, 0.044–4.928), pretreatment or posttreatment PET SUV (HR, 0.996; 95% CI, 0.730–1.395), total radiation dose (HR, 1.143; 95% CI, 0.734–1.779), or BED (HR, 1.578; 95% CI, 0.78–3.863). The median survival for the entire cohort was 20.1 months (95% CI, 18.7–28.4). The 1- and 2-year survivals were 85% and 45%, respectively. Differences in overall survival were evaluated on the basis of tumor size and clinical T stage. Increasing tumor size correlated with poorer overall survival (HR, 1.720; 95% CI, 1.154–2.563; $P = .008$). The median survival for T1 and T2 tumors was 20 months (95% CI, 20.1–31.6 months) and 16.7 months (95% CI, 10.8–21.2 months), respectively ($P = .073$). The 1- and 2-year survivals for T1 tumors were 87% and 55%, respectively.

FIGURE 2. Local control by T-stage grouping.

FIGURE 3. Overall survival by T-stage grouping.

The 1- and 2-year survivals for T2 tumors were 75% and 35%, respectively.

DISCUSSION

Lung tumor size is an important factor for predicting outcomes with lung SBRT for medically inoperable patients. In our series, increasing tumor size correlated with local failure. Patients with T1 tumors had a 90% local control rate at 2 years whereas those with T2 disease had an inferior 2-year local control rate of 70%. Small tumors (T1) also had a longer time to recurrence than did larger tumors (T2). Whether superior local control translates into a survival benefit is unclear. Our series demonstrates poorer overall survival when size was evaluated as a continuous variable. Smaller clinical T stage showed an estimated trend toward improved survival, although it did not quite reach statistical significance ($P < .07$), likely secondary to the small sample size and short follow-up. Our median follow-up time was relatively short at 12.5 months with 3 patients whose follow-up period was less than 4 months, which limits the capture of local and distant failure. With longer follow-up, a more clear survival advantage may be demonstrated with T1 tumors as more occult metastases may present in patients with T2 tumors.

The treatment of primary NSCLC with SBRT has been advocated in medically inoperable patients. The local control with lung SBRT has been shown to be equivalent to limited surgical resection. The incidence of local recurrence after limited surgical resection with either wedge resection or

segmentectomy has been reported to range from 10% to 27% in published series.^{2-5,13,14} Surgical data have shown that tumor T stage correlates with local failure, with most recurrences occurring within the first 2 years after resection.^{13,14} Published series using SBRT have reported similar local recurrence ranging from 10% to 30% with most recurrence occurring within the first year after treatment.^{8-11,15-17} Our series parallels other published data with an overall local recurrence rate of 17% at 2 years and a mean time to recurrence of approximately 12 months.

Tumor dose may play an important role in tumor sterilization and thus translate into improved local control and survival. Phase I and II studies have shown local control rates of 70% to 90% at 3 years and overall survivals of 50% to 60% using variable treatment regimens.^{8-11,15-17} Nominal total dose may underrepresent the biologic effectiveness of treatment; therefore, BED is often used as a surrogate to describe tumor dose. Our institutional cohort was treated with a median BED of 150 Gy (range, 78–180 Gy), which corresponds to doses reported in other published series. Initial studies from North America have advocated using a dose of 60 to 66 Gy delivered in 3 fractions (BED, 180 Gy). Yet other institutions from Europe and Asia have advocated using lower nominal doses of 45 Gy in 3 fractions (BED, 112.5 Gy), 50 Gy in 5 fractions (BED, 100 Gy), or 48 Gy in 4 fractions (105.6 Gy) with equivalent outcomes to larger BED schedules.¹³⁻¹⁷ Smaller fraction sizes may decrease rates of symptomatic

pneumonitis, chest wall pain, rib fracture, or skin injury. Our data also show acceptable tumor control with minimal toxicity. Grade II and III pneumonitis was seen in only 2 patients with a mean V20 of 8%. The incidence of chest wall pain was similar to that of other published reports, and only 2 patients had rib fractures.^{9,10}

The implications of inferior local control and possibly survival with larger tumors may greatly affect the treatment approach with lung SBRT. A phase I series from Indiana University⁸ included tumors 7 cm or larger in greatest diameter. The original study design included dose escalation to determine the maximum tolerated dose, stratified by tumor size (≤ 3 cm or > 3 cm). The maximum tolerated dose for small tumors was 60 Gy in 3 fractions, whereas the maximum tolerated dose for tumors 5 to 7 cm was 66 Gy in 3 fractions. Local recurrence was observed most commonly at fraction sizes less than 1200 cGy. There was no observed difference in local control or toxicity between T1 and T2 tumors, although the authors state the study was not powered to detect a difference. A follow-up phase II study from the University of Indiana¹¹ included 34 T1 tumors and 36 T2 tumors 7 cm or smaller. Small tumors were prescribed 60 Gy in 3 fractions and large tumors were prescribed 66 Gy in 3 fractions. A median follow-up of 50.2 months trended toward a worse survival for T2 tumors (24.5 months) compared with T1 tumors (38.7 months), although the difference was not significant statistically.

Chen and associates¹⁵ recently performed a retrospective evaluation of the efficacy of dose-individualized stereotactic body radiotherapy for patients with T1-3 NSCLC. A majority of patients were in stage T1. Sixty-five patients received 71.8 to 115.2 Gy of BED in 3.6- to 8.0-Gy daily fractions. No difference in local control or overall survival was seen between patients with T1, T2, or T3 tumors.

Inoue and colleagues¹⁶ retrospectively reviewed clinical outcomes for clinically diagnosed small primary lung cancers in medically inoperable patients. Primary lung cancer was not confirmed pathologically. A total of 115 patients were treated with SBRT using a total dose of 30 to 70 Gy in 2 to 10 fractions. Ninety-three percent of the patients had T1 tumors. There was no observed difference in local tumor response on the basis of tumor size. The 3-year overall survival for tumors 20 mm or smaller was 89% versus 60% for patients with tumors larger than 20 mm. This study suggests improved clinical outcome for smaller lesions although the authors point out this may partially be due to the inclusion of nonmalignant lesions in the cohort.

The impact of larger (T2) tumors with regard to treatment planning is currently unclear. Our data, as well as other series, suggest increased local failure compared with T1 tumors and possibly poorer overall survival. Dose and fractionation selection in our cohort was not influenced by tumor size but rather to limit treatment-related toxicity and meet dose constraints to the normal adjacent structures.

Although our data show no significant correlation with total dose or BED and local failure, dose escalation may be necessary above 60 Gy. Initial work from Indiana University^{8,11} prescribed larger tumors (> 7 cm) 66 Gy in 3 fractions, corresponding to a BED of approximately 200 Gy. The median fraction size in our cohort was 12 Gy, corresponding to a BED of 150 Gy. This dose differential may account for increased local failure for larger tumors in our patients. Another possibility is to address microscopic tumor extension. Prior studies have shown that CT imaging underestimates tumor extension based on pathologic correlates by as much as 12 mm.¹⁸ The standard approach in lung SBRT is to make the clinical target volume equivalent to the GTV, therefore specifically not targeting microscopic disease. Although dose falloff is sharp with SBRT, the beam penumbra is thought to be sufficient to sterilize microscopic disease. This concept may need to be reconsidered with larger tumor margins for treatment.

The detection of metastatic disease before treatment is important in predicting patient survival. In our series, mediastinal lymph node involvement was ruled out with enhanced CT or PET-CT. The sensitivity and specificity of PET-CT for detecting mediastinal lymph nodes has been reported to be 84%.¹⁹ Studies have also suggested that mediastinal nodal involvement may be higher in larger tumors.^{13,14,19} Clinical experience with lung SBRT in the treatment of primary NSCLC has shown less than 5% of isolated N1 or N2 nodal failures in the PET-CT era,²⁰ suggesting that surgical staging is not required in this subset of inoperable patients. Despite the potential utility of PET-CT for assessing mediastinal lymph nodes, the lack of mediastinal surgical staging may affect patient survival and distant failure by not detecting occult metastases. Thirty-four patients in our cohort underwent clinical staging with PET-CT and 6 patients did not, potentially affecting detection of metastatic disease at the time of treatment.

The utility of PET-CT scan with conventional radiotherapy has been widely established in predicting treatment outcome in NSCLC.^{21,22} Prospective studies have shown that posttreatment PET scan is highly predictive of survival compared with CT scans, tumor stage, or performance status.²³ In the setting of high doses per fraction, the PET response after treatment is likely different compared with conventional radiotherapy. Hoopes and associates²⁴ treated 58 patients with SBRT for early-stage lung cancer with SBRT. Twenty-eight patients had pretreatment and posttreatment PET-CT imaging. Fourteen percent of patients had percent abnormal activity in the primary tumor at 2 years without evidence of regional or distant failure. The University of Pittsburgh recently reported that in 28 patients treated with lung SBRT, persistently elevated FDG uptake was common despite tumor regression.²⁵ With a median follow-up of 1 year, patients with stable disease had a mean decrease in SUV of 28%, partial responders had

a mean decrease of 48%, and complete responders had a mean decrease of 94%. Our data show mixed posttreatment SUV response after SBRT. Sixty-six percent of patients with pretreatment and posttreatment PET-CT had a mean decrease in SUV of 56%, whereas 34% of our patients had a mean increase of 38%. There was no correlation between local tumor control and posttreatment SUV, although our findings are limited by the small number of patient with both pretreatment and posttreatment PET-CT.

The results of our SBRT study in patients with medically inoperable early-stage NSCLC are clinically equivalent to prior studies^{7-11,15-17} regarding local control and overall survival. Our data suggest that increased tumor size predicts local failure after SBRT. Similar to other single institutional data,^{8,11,15,16} larger tumor size suggests a clinically significant decrement in overall survival, although not statistically significant. Although our study has inherent limitations to retrospective studies, including selection bias and a small sample size, the findings bring into question the utility of SBRT for larger tumors. SBRT may not be an adequate local therapy for T2 tumors and thus alternative treatment modalities should be explored. Radiofrequency ablation as a primary modality or in combination with SBRT may overcome underlying biologic resistance and sterilize microscopic disease. Similarly, combined modality therapies such as concurrent chemotherapy or targeted agents may be appropriate for larger tumors to improve local control and overall survival.

CONCLUSIONS

SBRT using helical, arc-based radiation therapy is a well-tolerated and efficacious treatment for medically inoperable patients with early-stage peripheral NSCLC. Increasing tumor size correlates with poorer survival and local control. Patients with T2 tumors have higher rates of local recurrence than those with T1 tumors. Although not significant, T1 tumors trended toward improved overall survival. Tumor size is likely a significant factor in treatment response and may need to be taken into account during treatment planning. Options may include dose escalation, large treatment margins to cover microscopic disease, or combined modality therapies.

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