Title

Risk of Pneumonitis After Stereotactic Body Radiation Therapy in Patients With Previous Anatomic Lung Resection

Journal

Clinical Lung Cancer, 16(5)

ISSN

1525-7304

Authors

Hayes, Jason T
David, Elizabeth A
Qi, LiHong
et al.

Publication Date

2015-09-01

DOI

10.1016/j.cllc.2015.01.006

Peer reviewed

HHS Public Access

Author manuscript

Clin Lung Cancer. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

Clin Lung Cancer. 2015 September ; 16(5): 379–384. doi:10.1016/j.cllc.2015.01.006.

Risk of Pneumonitis after Stereotactic Body Radiation Therapy in Patients with Prior Anatomic Lung Resection

Jason T. Hayes, MD[1], **Elizabeth A. David, MD**[2], **LiHong Qi**[3], **Allen M. Chen, MD**[4], and **Megan E. Daly, MD**[1]

[1]University of California Davis Comprehensive Cancer Center Department of Radiation Oncology

[2]University of California Davis Section of Thoracic Surgery, Department of Surgery

[3]University of California Davis Department of Biostatistics

[4]University of California Los Angeles Department of Radiation Oncology

Abstract

Purpose/Objectives—Stereotactic body radiation therapy (SBRT) has emerged as a standard treatment for early stage, medically inoperable lung cancer. Limited data evaluate radiation pneumonitis (RP) risk for SBRT following prior anatomic lung resection (ALR). We assess the incidence of RP and all pulmonary toxicity (PT) in patients treated with lung SBRT following ALR and compare to patients without prior ALR.

Materials/Methods—We reviewed the medical records of 84 consecutively treated patients with T1-T2b NSCLC treated with 88 courses of SBRT for 94 lung tumors from January 2007-December 2014, including 17 patients with prior ALR. Rates of RP and all PT were compared between patients with and without prior ALR.

Results—At 18.3 months median follow-up (range 1.8- 85.6 months), crude grade 2+ RP rates were 5.9% and 2.8% for patients with and without prior ALR, respectively (p=0.51), with 2-year estimates of freedom from RP of 89% and 97% (p=0.51). Crude rates of all grade 2+ pulmonary toxicity were 11.8% and 2.8% (p=0.11), respectively, with 2-year freedom from PT of 97% and 84%, (p=0.11). The 2 cohorts were well matched by mean lung dose, lung V20 (p=0.86) and prescribed dose (p=0.75). Two-year estimates of local control, cause-specific survival, and OS were similar between cohorts.

Conclusions—Observed rates of pulmonary toxicity were low among all patients, with a trend toward increased grade 2-3 lung toxicity among patients with prior ALR. Prior ALR did not increase risk of grade 4-5 RP, and SBRT appears safe and effective in this population.

Corresponding Author: Megan Daly, MD, Department of Radiation Oncology, University of California, Davis, 4501 X Street, Sacramento, CA 95817, Phone: 1-916-734-5428, Fax: megan.daly@ucdmc.ucdavis.edu.

Conflicts of Interest and Source of Funding: none

Keywords

Non-small Cell Lung Cancer; SBRT; Lung resection

[1]Introduction

It is estimated that 188,000 new cases of non-small cell lung cancer (NSCLC) occurred in the United States in 2014, with 15% presenting as early stage disease. [1]. Surgical resection remains the standard-of-care for medically fit patients with stage I NSCLC. However, following surgical resection, as many as 7% of patients will recur locally and up to 12% may present with a second primary lung tumor within 8 years [2]. Often these patients are medically or technically inoperable due to the extent of previous resections and/or the presence of co-morbidities. Stereotactic body radiation therapy (SBRT) also known as Stereotactic Ablative Body Radiation (SABR) has emerged as a standard treatment option for early stage medically inoperable NSCLC, with excellent local control and acceptable toxicity, with several studies demonstrating no statistically significant decrease in lung function following SBRT [3-7].

Following lobectomy and pneumonectomy, pulmonary function is diminished from preoperative levels. Postoperatively, forced expiratory volume over 1 second (FEV1) and exercise capacity decrease by 15% and 16%, respectively, for lobectomy; FEV1 decreases by 35% and exercise capacity by 23% for pneumonectomy [7]. Hence minimizing further decrements in pulmonary function and avoiding radiation-induced lung toxicity is a priority. One well-documented side effect of radiation therapy is radiation pneumonitis (RP), manifesting as cough, fever, and shortness of breath at 6 weeks-12 months following radiation. Prior studies have identified clinical risk factors predisposing patients to RP, primarily in the setting of conventional fractionation, and include known pulmonary or cardiovascular disease, poor performance status, tumor location, age greater than 70 years old, and receipt of concurrent chemotherapy [8-12]. For SBRT, dosimetric parameters including volume of lung receiving ≥ 20 Gy (V20)>10%, mean lung dose >4 Gy and PTV volume also increase the risk of radiation pneumonitis [13-16].

Scant data address the risk of SBRT in post-pneumonectomy patients [17, 18], and none evaluate potential risks in prior lobectomy patients. The aim of the present analysis is to compare the rates of RP and rates of all lung toxicity following SBRT in patients with and without prior ALR.

Materials and Methods

Patients

Following Institutional Review Board Approval, the charts of all patients treated with SBRT for early stage NSCLC at the University of California Davis between January 2007-

[1]**ABBREVIATIONS:** SBRT- Stereotactic Body RadioTherapy: ALR- Anatomic Lung Resection; PT-Pulmonary Toxicity; RP-Radiation Pneumonitis; V20- Volume of tissue getting 20Gy; PTV- Planning Target Volume; NSCLC- Non Small Cell Lung Cancer; LC- Local Control; OS- Overall Survival; IMRT-Intensity Modulated RadioTherapy

December 2013 were retrieved and reviewed. Eighty-four consecutive patients were identified. Ten patients with presumed synchronous (6) or metachronous (4) primary lung cancers were included. Metachronous tumors were calculated as separate treatment courses, while synchronous primary tumors were considered a single treatment, leaving 88 evaluable courses of SBRT. Prior anatomic lung resection (ALR) including lobectomy (n=13), bilobectomy (n=1), and pneumonectomy (n=3) was documented for each patient. Median interval from prior ALR to SBRT was 115 months (range: 2-498 months). All pneumonectomies were performed on the left lung. The median number of segments resected was 5 (range 3-9). One patient treated with prior non-anatomic lung resection (wedge resection) was included in the control group. No patient had undergone prior segmentectomy. Patient clinical and disease characteristics, disease control, and toxicity were recorded for each patient. Patient characteristics are outlined in Table 1.

Simulation, Treatment Planning, and Delivery

Simulation was performed on the Phillips Brilliance Big Bore 16 slice scanner (Royal Philips Electronics, Amsterdam, The Netherlands) with 2 mm slice thickness. Patients were immobilized with either the Elekta body frame (Elekta AB, Stockholm Sweden) or the Elekta BodyFix (Elekta AB, Stockholm Sweden). Simulation was performed with computed tomography (CT) acquisition with abdominal compression and fluoroscopic assessment to ensure diaphragmatic excursion was limited to ≤1 cm. After December 2010 10 phase four dimensional CT (4DCT) was obtained in addition to free breathing CT.

For patients simulated without 4DCT, eccentric PTV margins of 10 mm in the craniocaudal directions and 5 mm radially were added to the GTV. Following 4DCT simulation, an ITV was created based upon the maximum intensity projection (MIP) and a uniform 5 mm PTV was added. Target dose ranged from 40-60 Gy in 3-8 fractions, with plans designed to deliver 100% of the prescription dose to a minimum of 95% of the PTV. Heterogeneity corrections using a superposition/convolution algorithm were applied starting in March of 2011, and cases prior were calculated without heterogeneity correction. The most common fractionation schedules were 50 Gy in 4 fractions, 54 Gy in 3 fractions and 60 Gy in 3 fractions, with no significant difference in selected schedule between the ALR and non-surgical cohorts (Table 1). A variety of planning techniques were employed, based upon the specific clinical scenario, including static non-coplanar beams (n=49), fixed field IMRT (n=28), and volume modulated arcs (n=17). The volume of lung tissue receiving ≥20 Gy (V20) was limited to <10% when possible. No modification to the dose constraints were used for patients with prior ALR. Treatment was delivered with abdominal compression, without respiratory gating, on an Elekta linear accelerator (Elekta AB, Stockholm Sweden). Image guidance was performed by onboard kV cone-beam CT (CBCT) imaging, with 3D anatomy match to the planning CT scan. Fluoroscopy was assessed prior to each fraction to ensure diaphragmatic excursion was limited to ≤1 cm.

Clinical Outcome Assessment and Statistics

Patient charts were retrospectively reviewed for disease control, survival, and acute and late toxicities. Treatment plans and dose volume histograms were retrieved and reviewed. Toxicities were graded according to the Common Terminology Criteria for Adverse Events

(CTCAE) v.4.0. Rates of grade 2+ and grade 3+radiation pneumonitis (RP) and rates of any pulmonary toxicity (PT) (including RP, post-obstructive pneumonias, bronchial strictures, hemoptysis, or clinically evident pulmonary fibrosis) were compared between patients with and without prior ALR. Crude rates of RP and PT were compared using Fisher's exact test. Local failure (LF) was defined as time from start of treatment to time an in-lobe failure was documented on imaging. Regional failure (RF) was defined as time from start of treatment to the time an ipsilateral lung or nodal failure was documented on imaging. Actuarial estimates of freedom from RP (FFRP), local control (LC), Regional control (RC) and overall survival (OS) were calculated with the Kaplan-Meier method and compared between cohorts via the log rank method. Differences in PTV volume, lung dosimetric parameters, histology, and disease stage were compared with an unpaired t-test. Simple logistic regression models were used to investigate the association between PT or RP and mean lung dose, volume of lung receiving 20 Gy, 30 Gy, and 5 Gy (V20, V30, and V5), PTV volume and prior ALR (yes or no), respectively. Unadjusted odds ratio (OR), corresponding 95% confidence intervals (CI) and P values were obtained. Due to the limited number of events for lung toxicity and radiation pneumonitis, multiple logistic regressions were unable to be performed. Analysis was performed with Graphpad (Graphpad Software Inc, La Jolla, CA) and SAS version 9.3 (SAS Institute, Cary, NC USA). All statistical tests were two sided and $p < 0.05$ was considered statistically significant.

Results

Median follow-up was 18.3 months (range 1.8-85.6 months). Three patients who had follow-up <3 months were lost secondary to death from metastatic disease (n=2) or cancer and treatment unrelated causes (n=1). These were kept in our study to prevent biasing overall survival results. The prior ALR and control cohorts were well-matched by gender (p=0.06) and prescribed dose (p=0.75), with a trend toward more women in the prior-ALR group (Table 1). The cohorts were also well matched by mean lung dose (3.9 Gy vs 4.2 Gy), lung V20 (4.2% vs 4.4%; p=0.87), lung V30 (2.78 vs 2.817; p= 0.93), V5 (21.97 vs 21.14; p=.72) and mean PTV (27.5 cc vs 34.9 cc; p=0.36). There was significantly more squamous cell carcinoma among patients with prior ALR (41% vs 21%; p=0.0001), and more T1b (as compared to T1a) tumors in the cohort without prior ALR (p=0.04).

Grade 2+ RP was identified in 1 ALR patient (5.9%) and 2 non-ALR patients (2.8%) (p=0.54) at a median of 6.6 months. Grade 2+ PT was identified in 2 ALR patients (11.8%) and 2 non-ALR patients (2.8%) (p=0.14) at a median of 5 months (range 0.4 - 14.8 months). Both cases of PT in the ALR group occurred in lobectomy patients. The incidence of RP and number of patients undergoing bilobectomy and pneumonectomy were too low to stratify by resection type. The median number of resected segments in the entire surgical cohort was 5 (range: 3-9), and the median among the patients developing PT was also 5. The 2-year Kaplan-Meier estimates of freedom from grade 2+ RP and PT for ALR and non-ALR patients were 89% and 97% (p=0.51) and 84% vs 97% (p=0.11) (Fig 1a-b). Non-RP lung toxicity included one grade 4 post-obstructive pneumonia.

The 2 year Kaplan-Meier estimate of LC for the entire population was 94.2%, with estimates of 100% for the prior ALR group and 92.9% for the non-ALR group (p=0.28) (Figure 2).

Corresponding 2-year estimates of RC, CSS, and OS were 93.3% vs 87.4% (p=0.61), 88.2% vs 90.5% (p=0.32), and 88.2% vs 73.8% (p=0.71) (Figure 3).

Simple logistic regression models identified that PT was significantly associated with lung V5 (OR = 1.08, 95% CI 1.01 – 1.15, P = 0.02), and the risk of RP was significantly associated with mean lung dose (OR = 1.48, 95% CI 1.02 – 2.13, P = 0.03). There was a borderline significant trend for the risk of RP and lung V5 (OR = 1.07, 95% CI 1.00 – 1.14, P = 0.05) and lung V20 (OR = 1.23, 95% CI 0.98 - 1.53, P = 0.07), respectively. Lung V30 (p=0.46), PTV size (p=0.86), and prior ALR (p=0.54) did not predict for development of RP.

Discussion

Anatomic resection with lobectomy, bilobectomy, or pneumonectomy constitutes the standard-of-care for medically operable early stage NSCLC. However, with local recurrence rates of approximately 7% and rates of metachronous primary lung tumors approaching 12% [2] many patients will eventually require additional local therapy for lung cancer. Frequently, additional surgical resection is not possible for these patients due to already compromised lung function from prior surgery or progressive medical comorbidities. In this setting, SBRT offers a potentially curative treatment option.

RP is a well-documented but relatively rare sequela of SBRT, with reported rates of grade 2+ RP of 9.3% [12] and of grade 3+ RP of 2-3.6% [4, 19]. The increased risk of fatal RP for patients undergoing conventionally fractionated radiotherapy following pneumonectomy is well documented, primarily in the mesothelioma literature, with fatal pneumonitis reported from 9.5% up to 46% of treated patients when rigorous lung dose-volume constraints are not observed [20-22].

However, only scant data have emerged evaluating the post-surgical risk of SBRT, primarily in the pneumonectomy population, and suggest higher rates of grade 3+ RP than historical reports for nonpneumonectomy patients. Haasbeek and colleagues analyzed 15 patients status-post pneumonectomy who subsequently underwent SBRT for a new stage 1 NSCLC, identifying grade ≥3 pneumonitis in 2 of 15 patients (13.3%) [18]. Similarly, Thompson and colleagues report outcomes for a cohort of 13 patients with prior pneumonectomy subsequently treated with SBRT, identifying 2 cases of grade 3+ pneumonitis (15.4%) [17].

The reduced parenchymal lung volume and function following lobectomy or bilobectomy could similarly be predicted to more modestly increase risk of RP following SBRT. Prior studies have documented a compensatory response of remaining tissue following ALR that increases lung volume [23]. This originally was attributed primarily to hyperinflation of the alveolar ducts, but there is growing evidence that there is also an increase in the functional lung volume with CT attenuation showing Hounsfield units similar to normal lung tissue [24]. In the setting of pure hyperinflation, the reduced parenchymal lung volume and function following lobectomy or bilobectomy could more modestly increase risk of RP following SBRT. However, a compensatory increase in functional lung volume may theoretically mitigate some of this concern.

A prior multi-institution analysis suggests that no threshold lower limit for pulmonary function testing (PFT) that precludes safe use of SBRT exists, with no increased risk of RP among poor-PFT patients, and that patients with the worst pre-treatment PFTs actually appreciated improvements in PFT results on average following SBRT [25]. However, these results may not apply specifically to the post-surgical setting. Post-surgical scarring could also theoretically increase rates of other uncommon SBRT-associated lung toxicities such as bronchial scarring/stenosis, hemoptysis, strictures, and post-obstructive pneumonias. However, no published studies have specifically analyzed the relative risk of RP and other lung toxicities in post-ALR patients.

Logistic regression demonstrated statistically significant association between bilateral mean lung dose and risk of RP, and a strong trend toward an association with bilateral lung V5 and V20. Similarly, overall risk of PT was significantly associated with lung V5. The number of events was too low to generate robust recommendations for lung constraints from our data. Prior studies assessing RP risk following SBRT have generated conflicting results. Baker *et al* analyzed a large series of 297 courses of lung SBRT to comprehensively assess dosimetric predictors of RP. In univariable analysis, both V5 and V13 were predictive of RP, while in multivariable analysis no dosimetric factors clearly correlated to development of RP [26]. By contrast, Bongers and colleagues assessed a cohort of 79 patients with either large tumors (n=69) or prior bilobectomy or pneumonectomy (n=13) and identified contralateral mean lung dose and ITV volume as strong predictors of grade ≥3 RP [27]. Similarly, Guckenberger *et al* report a detailed dosimetric analysis from 59 consecutive patients treated with lung SBRT, and identified ipsilateral mean lung dose and volumes of the lung exposed to minimum doses between 2.5 and 50 Gy correlated to RP risk [28].

To our knowledge, this is the first published series directly comparing RP and other lung toxicities between patients with and without prior ALR treated with SBRT. We identified relatively modest rates of grade 2+ RP and all PT in both cohorts, with a trend toward increased PT risk in prior-ALR patients that did not reach statistical significance, with grade 2+ PT identified in 11.8%. However, these relatively low rates of RP and PT among prior ALR patients and the absence of grade 4-5 toxicity in the surgical cohort suggests SBRT remains a safe and effective treatment option for these patients. Cancer specific outcomes including LC, RC, and CSS were similar between cohorts, as was OS, and are consistent with historical reports.

There are a number of limitations to the current study. Beyond its retrospective nature, our patient numbers are too low to more rigorously assess whether the lung constraints used for lung SBRT with intact lungs should be applied to patients with prior lung resection. Both our total patient numbers and low complication rate precluded further stratification by resection type. Larger analyses could confirm our noted trend toward a slight increase in grade 2+ RP among patients with prior ALR and potentially establish volumetric lung constraints specific to this population. While our median follow up of 18 months should be sufficient to capture most cases of RP, other long-term lung toxicities may develop beyond 18 months, and longer follow up is desirable.

Conclusions

Observed rates of RP and PT were low among all patients, with a trend toward increased grade 2+ PT among prior ALR patients that did not reach statistical significance. The generally low rates of toxicity in both cohorts suggest SBRT is safe and effective following ALR when appropriate lung constraints are followed. Larger analyses are needed to confirm the risk of RP among prior ALR patients and to establish optimal lung DVH parameters for this cohort.

Acknowledgements

We acknowledges support from the Biostatistics Shared Resource of the UC Davis Cancer Center Support Grant, P30CA093373-11

References

1. American Cancer Society. Cancer Facts & Figures. American Cancer Society; Atlanta: 2014. 2014
2. Martini N, et al. Incidence of local recurrence and second primary tumors in resected stage I lung cancer. J Thorac Cardiovasc Surg. 1995; 109(1):120–9. [PubMed: 7815787]
3. Baumann P, et al. Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. J Clin Oncol. 2009; 27(20): 3290–6. [PubMed: 19414667]
4. Timmerman R, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA. 2010; 303(11):1070–6. [PubMed: 20233825]
5. Fakiris AJ, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. Int J Radiat Oncol Biol Phys. 2009; 75(3):677–82. [PubMed: 19251380]
6. Ohashi T, et al. Differences in pulmonary function before vs. 1 year after hypofractionated stereotactic radiotherapy for small peripheral lung tumors. Int J Radiat Oncol Biol Phys. 2005; 62(4):1003–8. [PubMed: 15990001]
7. Win T, et al. The effect of lung resection on pulmonary function and exercise capacity in lung cancer patients. Respir Care. 2007:720–6. [PubMed: 17521461]
8. Ali MK, et al. Regional and overall pulmonary function changes in lung cancer. Correlations with tumor stage, extent of pulmonary resection, and patient survival. J Thorac Cardiovasc Surg. 1983; 86(1):1–8. [PubMed: 6865454]
9. Baumann P, et al. Stereotactic body radiotherapy for medically inoperable patients with stage I non-small cell lung cancer - a first report of toxicity related to COPD/CVD in a non-randomized prospective phase II study. Radiother Oncol. 2008; 88(3):359–67. [PubMed: 18768228]
10. Inoue T, et al. Stereotactic body radiotherapy for pulmonary metastases. Prognostic factors and adverse respiratory events. Strahlenther Onkol. 2013; 189(4):285–92. [PubMed: 23420546]
11. Mehta V. Radiation pneumonitis and pulmonary fibrosis in non-small-cell lung cancer: pulmonary function, prediction, and prevention. Int J Radiat Oncol Biol Phys. 2005; 63(1):5–24. [PubMed: 15963660]
12. Chang JY, et al. Clinical outcome and predictors of survival and pneumonitis after stereotactic ablative radiotherapy for stage I non-small cell lung cancer. Radiat Oncol. 2012; 7:152. [PubMed: 22963661]
13. Hope AJ, et al. Modeling radiation pneumonitis risk with clinical, dosimetric, and spatial parameters. Int J Radiat Oncol Biol Phys. 2006; 65(1):112–24. [PubMed: 16618575]
14. Vogelius IR, Bentzen SM. A literature-based meta-analysis of clinical risk factors for development of radiation induced pneumonitis. Acta Oncol. 2012; 51(8):975–83. [PubMed: 22950387]

15. Barriger RB, et al. A dose-volume analysis of radiation pneumonitis in non-small cell lung cancer patients treated with stereotactic body radiation therapy. Int J Radiat Oncol Biol Phys. 2012; 82(1): 457–62. [PubMed: 21035956]
16. Matsuo Y, et al. Dose--volume metrics associated with radiation pneumonitis after stereotactic body radiation therapy for lung cancer. Int J Radiat Oncol Biol Phys. 2012; 83(4):e545–9. [PubMed: 22436782]
17. Thompson R, et al. Stereotactic body radiotherapy in patients with previous pneumonectomy: safety and efficacy. J Thorac Oncol. 2014; 9(6):843–7. [PubMed: 24828663]
18. Haasbeek CJ, et al. Outcomes of stereotactic radiotherapy for a new clinical stage I lung cancer arising postpneumonectomy. Cancer. 2009; 115(3):587–94. [PubMed: 19130457]
19. Lagerwaard FJ, et al. Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. Int J Radiat Oncol Biol Phys. 2012; 83(1):348–53. [PubMed: 22104360]
20. Lagerwaard FJ, et al. Curative radiotherapy for a second primary lung cancer arising after pneumonectomy -- techniques and results. Radiother Oncol. 2002; 62(1):21–5. [PubMed: 11830309]
21. Rice DC, et al. Dose-dependent pulmonary toxicity after postoperative intensity-modulated radiotherapy for malignant pleural mesothelioma. Int J Radiat Oncol Biol Phys. 2007; 69(2):350–7. [PubMed: 17467922]
22. Allen AM, et al. Fatal pneumonitis associated with intensity-modulated radiation therapy for mesothelioma. Int J Radiat Oncol Biol Phys. 2006; 65(3):640–5. [PubMed: 16751058]
23. Esophageal and Esophagogastric Junction Cancers. NCCN Guidelines. 2013 Version 1.
24. Ueda K, et al. Compensation of pulmonary function after upper lobectomy versus lower lobectomy. J Thorac Cardiovasc Surg. 2011; 142(4):762–7. [PubMed: 21679975]
25. Guckenberger M, et al. Is there a lower limit of pretreatment pulmonary function for safe and effective stereotactic body radiotherapy for early-stage non-small cell lung cancer? J Thorac Oncol. 2012; 7(3):542–51. [PubMed: 22258475]
26. Baker R, et al. Clinical and dosimetric predictors of radiation pneumonitis in a large series of patients treated with stereotactic body radiation therapy to the lung. Int J Radiat Oncol Biol Phys. 2013; 85(1):190–5. [PubMed: 22929858]
27. Bongers EM, et al. Predictive parameters of symptomatic radiation pneumonitis following stereotactic or hypofractionated radiotherapy delivered using volumetric modulated arcs. Radiother Oncol. 2013; 109(1):95–9. [PubMed: 24183862]
28. Guckenberger M, et al. Dose-response relationship for radiation-induced pneumonitis after pulmonary stereotactic body radiotherapy. Radiother Oncol. 2010; 97(1):65–70. [PubMed: 20605245]

Clinical Practice Points

Following surgical resection for early stage lung cancer, as many as 7% of patients will recur locally and up to 12% may present with a second primary lung tumor within 8 years. Often these patients are medically or technically inoperable due to the extent of previous resections and/or the presence of comorbidities. Stereotactic body radiation therapy (SBRT) is often considered as a treatment option for these patients.

Following lobectomy and pneumonectomy, pulmonary function is diminished from preoperative levels; hence, avoiding radiation-induced lung toxicity is a priority. A common side effect of radiation therapy is pneumonitis, and following conventionally fractionated radiotherapy, increased risks of pneumonitis with prior pneumonectomy are well-documented.

Despite the frequency second primaries potentially suitable for SBRT following prior lung surgery, scant published data address potential risks. A total of 2 small case series (references 17 -18) address the risk of SBRT in post-pneumonectomy patients, and none specifically evaluate potential risks in lobectomy patients. We present an analysis of 84 consecutively treated patients with T1-T2b NSCLC treated with 88 courses of SBRT for 94 lung tumors, including 17 patients with prior lung resection. Observed rates of pulmonary toxicity were low, with a trend toward increased grade 2-3 lung toxicity among patients with prior ALR. Prior ALR did not increase risk of grade 4-5 RP, and overall SBRT appears safe and effective in this population. Our data build on the scant available data on this topic, and provide additional reassurance that SBRT is reasonably safe in this population.

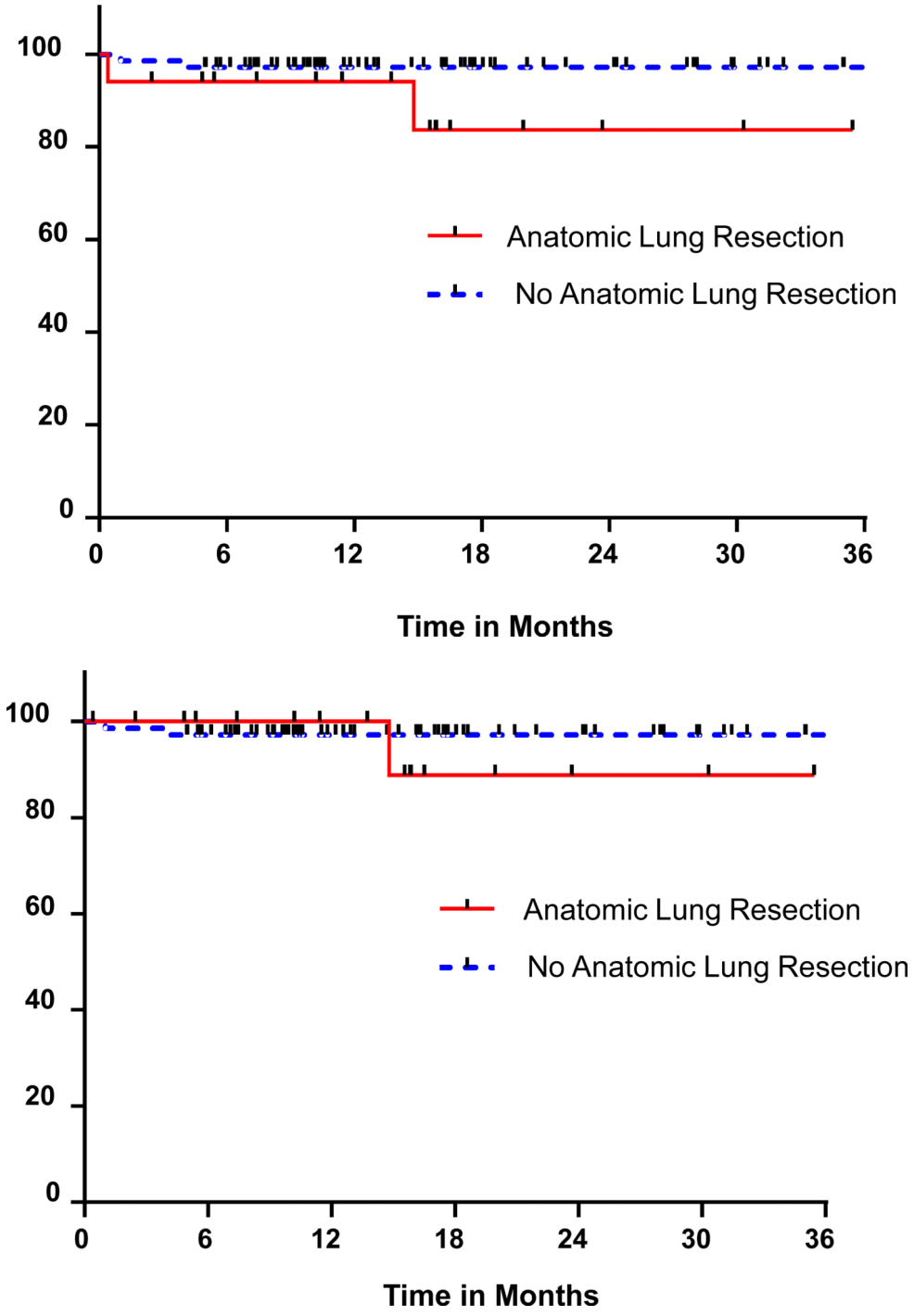

Figure 1.

a-b: Actuarial rates of radiation pneumonitis (a) and all pulmonary toxicity (b) in prior anatomic lung resection (solid line) and control (dashed line) patients

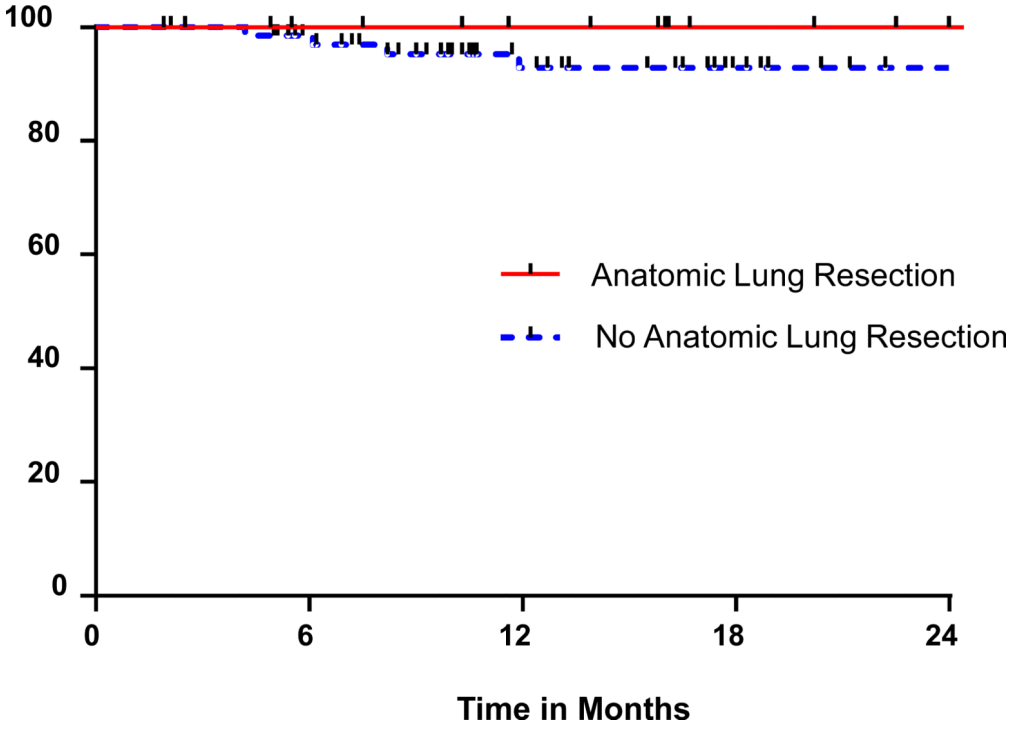

Figure 2.
Actuarial estimates of local control in prior anatomic lung resection (solid line) and control (dashed line) patients

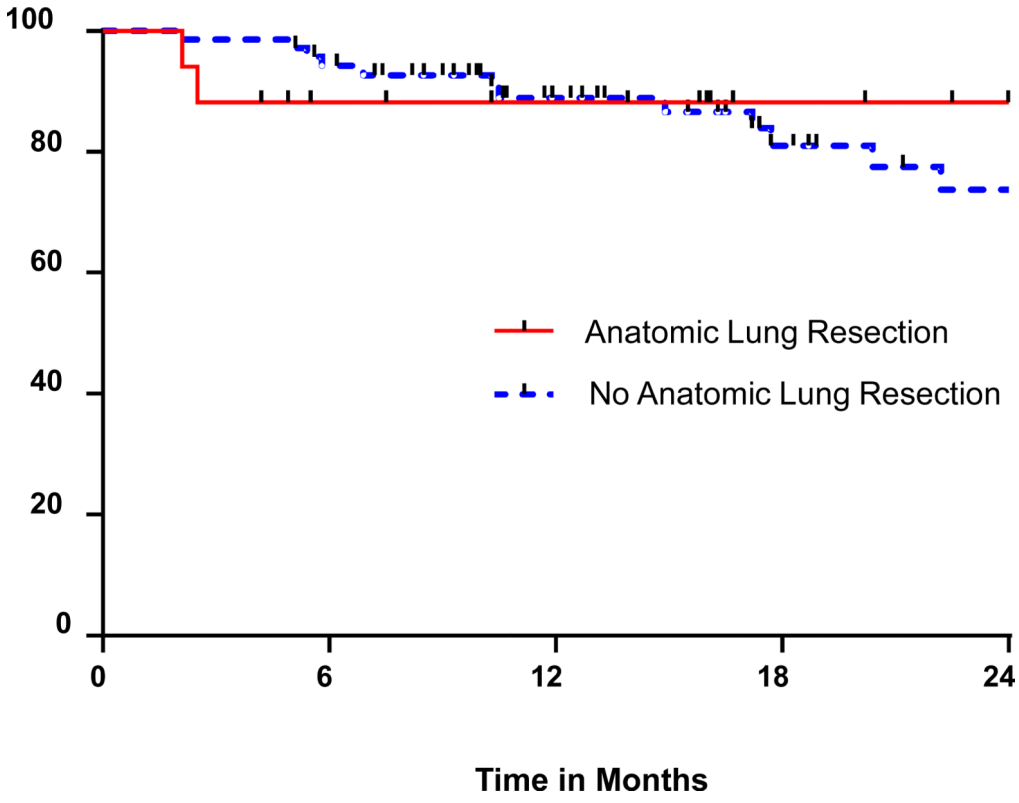

Figure 3.
Actuarial estimates of overall survival in prior anatomic lung resection (solid line) and control (dashed line) patients

Table 1

Patient Characteristics

Characteristic	Prior Resection N= 17 (%)	No Prior Resection N= 71 (%)	P value
Age	72.3	75.8	0.18
Gender- Female	13 (76%)	36 (51%)	0.06
Pathology			
Squamous cell	7 (41%)	15 (21%)	0.0001
Adenocarcinoma	8 (47%)	45 (63%)	0.22
Other	2 (12%)	11 (15%)	0.70
Prescription Dose (Gy)	53.2	53.6	0.75
48-50 Gy in 4	7 (41%)	20 (28%)	0.30
50-55Gy in 5	2 (12%)	14 (20%)	0.45
54-60Gy in 3	4 (24%)	32 (45%	0.77
60Gy in 5	4 (24%	0 (0%	0.32
60Gy in 8	1 (6%)	1 (1%)	0.27
T-stage			
T1a No. (%)	13 (76%)	36 (51%)	0.06
T1b No. (%)	1 (6%)	21 (30%)	0.04
T2 No. (%)	3 (18%)	14 (20%)	0.85
Lung V20	4.2%	4.4%	0.87
Lung V5	21.9%	20.8%	0.72
Lung V30	2.8%	2.8%	0.93
Mean Lung Dose (Gy)	3.9	4.2	0.77
Mean planning target volume (ml^3)	27.5	34.9	0.36

Abbreviations: Gy: Gray; V20: Volume receiving 20 Gy; V5: Volume receiving 5 Gy; V30: Volume receiving 30 Gy