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Purpose/Objective(s): To assess the outcome of early-stage non-small cell lung cancer (NSCLC) treated with single- versus five-fraction stereotactic body radiation therapy (SBRT) at two institutions.
Materials/Methods: In our study, peripheral early-stage NSCLC cases treated with either a median dose of 30 Gy (IQR 30-30, BED 120-120) in a single fraction or a median dose of 50 Gy (IQR 50-50, BED 100-100) in five fractions were included. Data were retrospectively collected in an institutional review board-approved database. Statistical software was used for statistical analysis.
Results: Of total 163 lesions treated between 2007 and 2015, 65 received single-fraction SBRT and 98 received five-fraction SBRT. The five-fraction SBRT cohort had significantly smaller tumors ($p<0.001$), and a larger tumor size was a prognostic factor for worse survival (HR 1.28, $P=0.029$). No grade 3 or higher toxicity was observed in the single-fraction SBRT cohort, while a single grade 3 symptomatic pneumonitis was seen in the five-fraction SBRT cohort. Propensity score matching resulted in the cohort of 90 patients with median follow-up of 26.5 months (IQR 16.2-34.7) for the single-fraction cohort and 34.0 months (IQR 21.0-48.0) for the five-fraction cohort ($p=0.054$). There were no statistically significant differences between these two regimens in overall survival ($p=0.19$), progression-free survival ($p=0.89$), local failure ($p=0.38$), and nodal or distant failure ($p=0.76$) at 2 years.
Conclusion: The single- and five-fraction SBRT cohorts had comparable outcomes and were well tolerated. Increasing tumor size was associated with worse survival. Both regimens are reasonable treatment options for early-stage peripheral NSCLC.
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Impact of Tumor Location & Dosimetric Predictors for Chest Wall Toxicity in Single Fraction SBRT for Stage I Non-Small Cell Lung Cancer

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Purpose/Objective(s): Single fraction stereotactic body radiation therapy (SF-SBRT) is an acceptable regimen for the treatment of peripheral Stage I Non-Small Cell Lung Cancer (NSCLC). Rates of chest wall toxicity (CWT) reported by phase II trials did not stratify by distance of tumor to chest wall (CW) and dosimetric parameters to limit CWT are not well defined. We sought to determine the relationship of tumor location and dosimetric parameters with CWT in SF-SBRT for peripheral Stage I NSCLC.
Materials/Methods: An institutional review board-approved prospective SBRT registry of 1,462 patients (pts) was used to identify pts treated with 30 Gy or 34 Gy in one fraction, on or off relevant protocols. Tumors were ≤ 5 cm, node-negative, and ≥ 2 cm from the proximal tracheo-bronchial tree. The ribs and CW were retrospectively contoured (CW as a 3 cm soft-tissue structure between the sternum and vertebral body). Gross tumor volume was measured as abutting, ≤ 1 cm, 1-2 cm or > 2 cm from the CW. CWT was graded according to CTCAE 3.0 criteria. Rates of CWT were compared using unpaired t-test. Logistic regression analysis was used to identify tumor and dosimetric parameters associated with CWT.
Results: This study included 138 pts treated with SF-SBRT to 146 lesions. Median follow-up was 23.8 months (34.7 months for living pts). There were 80 pts (55%) treated with 30 Gy and 66 pts (45%) treated with 34 Gy. The rate of CWT was 30.6% for lesions abutting CW, 8.2% for lesions ≤ 1 cm from CW, 3.8% for lesions 1-2 cm from CW, and 5.7% for lesions > 2 cm from CW. Grade ≥ 3 CWT for the whole cohort was modest (1.4%). Tumor abutment (OR 6.5; $p=0.0005$), BMI (OR 1.1; $p=0.02$), rib D1cc (defined as dose to 1 cc) (OR 1.01 per Gy; $p=0.03$), CW D1cc (OR = 1.08 per Gy; $p=0.03$), and CW D5cc (OR 1.10 per Gy; $p=0.01$) were significant predictors for CWT on univariate analysis. Tumor abutment was the only significant predictor for CWT (OR 7.5; $p=0.007$) on multivariate analysis. CWT remained low until a dose threshold and then increased more rapidly. CWT occurred in only 1 out of 40 pts with CW D5cc < 18 Gy (defined as dose to 5 cc less than 18 Gy), while our model suggested a 15% risk of CWT with D5cc of 27.2 Gy to the CW. CWT occurred in only 1 out of 39 pts with rib D1cc < 19 Gy, while our model suggested a 15% risk of CWT with D1cc of 30.2 Gy to the rib.
Conclusion: The rate of CWT is significantly associated with distance from the CW. When considering only lesions adjacent to the CW, the rate of CWT in this series (30.6%) does not appear to exceed rates in the published fractionated SBRT literature (20-33%). This suggests location adjacent to the CW should not be a contraindication to SF-SBRT. Rib D1cc and CW D1cc and D5cc may be used as predictors of CWT rates, as noted in this model. As most CWT is low-grade and self-limited, these dosimetric parameters should be utilized as a guideline, rather than an absolute constraint.
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Impact of Comorbidities on Acute Toxicity in Patients Receiving Radiation Therapy for Locally Advanced Lung Cancer

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Purpose/Objective(s): Patients with advanced lung cancer often have multiple medical comorbidities; however, it is not well known if comorbidity burden impacts tolerance of thoracic radiation treatment (TRT). We hypothesized that patients with more comorbidities are more likely to experience acute toxicity from TRT for locally advanced lung cancer.
Materials/Methods: We queried two patient databases: data from four prospective institutional investigator-initiated trials (IIT) as well as data from a large multicenter state-wide quality consortium. To assess comorbidities, we used the Charlson Comorbidity Index (CCI) for the IIT cohort and created a Comorbidity Index (CI) using similar, available data for the consortium cohort. Logistic regression was used to determine the relationship between comorbidity indices and radiation-induced toxicities, specifically grade≥ 2 esophagitis and pneumonitis. Adjustments were made for PTV volume, concurrent chemotherapy, and radiation dose to organs at risk. Weighting variables were applied for consortium patients for modeling pneumonitis outcome because of heterogeneity in follow-up time.
Results: A total of 1188 patients were analyzed in the IIT and consortium cohorts (112 and 1076, respectively), with average age 65 and 67 years and PTV volume of 465 and 369 mL. Total incidence of grade ≥ 2 radiation pneumonitis was 13.5% and 6.8%, and grade ≥ 2 esophagitis was 41.4% and 54.3%, respectively, for the IIT and consortium cohorts. Mean CCI for the IIT cohort was 3.7; mean CI for the consortium cohort was 1.5. The data were concordant that there is no evidence linking comorbidity indices to any toxicity outcome (Table 1). Esophagitis was significantly associated with concurrent chemotherapy ($p<0.0001$ in the consortium cohort, NS in the IIT cohort) and mean esophageal dose ($p<0.0001$ in the consortium cohort and $p=0.04$ in the IIT cohort). Pneumonitis was also significantly related to mean lung dose in the IIT cohort ($p=0.04$).

Abstract TU_30_3622; Table 1 Effect of Clinical Variables on Radiation-Induced Toxicities

Odds Ratio (OR) and p-value (p)	Esophagitis				Pneumonitis			
	Consortium		IIT		Consortium		IIT	
Variable	OR	p	OR	p	OR	p	OR	p
PTV vol.	1.0	0.92	0.91	0.28	1.1	0.17	1.1	0.43
Conc. Chemo	2.5	**<0.0001**	5.8	0.11	1.1	0.89	1.3	0.81
Mean Esophagus Dose	1.1	**<0.0001**	1.1	**0.04**	-	-	-	-
Mean Lung Dose	-	-	-	-	1.1	0.11	1.2	**0.04**
Comorbidity Index	1.0	0.43	0.94	0.67	1.0	0.98	0.68	0.11

Conclusion: This is the largest study using prospectively-collected data of lung cancer patients treated with definitive TRT evaluating comorbidity burden and radiation-induced acute toxicity. As an independent variable, comorbidity indices are not associated with higher rates of esophagitis or pneumonitis in lung cancer patients undergoing TRT. This suggests that treatment-related rather than patient-specific factors are most important in determining the toxicity profile for these patients.

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Effect of Adding Induction or Adjuvant Chemotherapy to Concurent Cheomradiation Therapy for Stage III Non-Small Cell Lung Cancer on Radiation Pneumonitis Assessed by Lung FDG Uptake and Clinician and Patient-Reported Symptoms

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Purpose/Objective(s): We analyzed whether receipt of induction chemotherapy (ICT) or adjuvant chemotherapy (ACT) influenced radiation pneumonitis (RP) grade as rated by physicians, and by patient-reported outcomes (PROs), and lung uptake of ^{18}F-fluorodeoxyglucose (FDG) among patients treated with concurrent chemoradiation therapy for stage III non-small cell lung cancer (NSCLC).

Materials/Methods: Subjects were 131 patients who received either ACT or ICT in addition to concurrent chemoradiation (CCRT) or CCRT alone as part of a randomized clinical trial involving both IMRT and protons; information on RP grade, mean standardized uptake values for FDG (SUVmean), and PRO scores were obtained from all patients and compared at various time points during and after therapy.

Results: Analysis of all patients as well as case-matched patients revealed that receiving either ACT or ICT in addition to CCRT resulted in significantly increased SUVmean at 4-6 months after CCRT. For all patients, those that received ACT or ICT in addition to CCRT had an SUVmean of 0.83 compared to an SUVmean of 0.73 for those that received CCRT alone (p = .04). In the case matched analysis, the ACT or ICT in addition to CCRT group had a SUVmean of 0.86, while the CCRT alone group had a SUVmean of 0.75 in the CCRT group (p = .04). A comparison of all patients treated with ICT plus CCRT with all patients treated with only CCRT revealed an increased SUVmean 4-6 months after CCRT. The SUVmean was 0.84 in the ICT plus CCRT group and 0.73 in the CCRT only group. In the analysis of all patients and in the case matched analysis, there was no statistically significant difference between the SUVmean of the ACT plus CCRT group and the CCRT alone group at any time period. There was no statistically significant difference in PRO or RP grade scores between the CCRT alone group and the CCRT plus ACT or ICT group, the CCRT plus ACT group, or CCRT plus ICT group. However, there was a trend for patients who received ICT to have higher RP scores at 4-6 months compared to patients treated with CCRT alone. The results of radiation modality on RP grade, SUVmean and PRO are presented elsewhere.

Conclusion: Adding sequential chemotherapy to CCRT, particularly ICT, was associated with increased SUVmean at 4-6 months after treatment. Since previous studies have shown that SUVmean is associated with RP and there was a trend for increased RP grade in patients treated with ICT, more randomized controlled trials are needed to see if the addition of ICT to CCRT causes an increase in severity of RP.

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Postoperative Radiation Therapy Has No Effect in Improving the Survival of Patients Aged ≤55 Years with Completely Resected Pathological Stage IIIA-N2 Non-Small-Cell Lung Cancer

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Purpose/Objective(s): For patients with completely resected pathological stage IIIA−N2 non-small cell lung cancer (NSCLC), studies has shown that postoperative radiotherapy (PORT) does not improve survivals of elderly patients (>65 years). However, the role of PORT for younger patients is not well defined. This study is to evaluate the effect of PORT on survivals as well as tumor control in patients ≤65 years.

Materials/Methods: Between Jan. 2003 and Dec. 2015, patients, ≤65 years, with pIIIA−N2 NSCLC after complete resection in our single institution were retrospectively analyzed. The effect of PORT on overall survival (OS), disease free survival (DFS), loco-regional recurrence free survival (LRFS), and distant metastasis free survival (DMFS) was evaluated with Kaplan-Meier method and log-rank test. Multivariable Cox regression analysis was used to identify independent risk factors for death. Pearson chi-square test was used to compare the constituent ratios between groups. Propensity score-matched (PSM) analysis was conducted to generate comparable study arms. Statistically significant difference was set as $p<0.05$.