including dosimetric information, is needed to access toxicities of heart and proximal bronchial tree in thoracic SBRT.

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Addition of Surgery After Radiation Significantly Improves Survival in Stage IIIB Non-Small Cell Lung Cancer: A Population-Based Analysis

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Purpose/Objective(s): Traditionally, stage IIIB non-small cell lung cancer (NSCLC) has been considered to be a surgically unresectable disease. Chemoradiation has become a standard treatment approach. However, in select patients, neoadjuvant treatment has been able to convert unresectable disease to resectable disease. Limited work, either retrospective or prospective, has been done to investigate whether or not there is a cause-specific mortality (CSM) or all-cause mortality (ACM) benefit to adding surgery following neoadjuvant treatment for stage IIIB NSCLC.

Materials/Methods: We extracted patients with Stage IIIB NSCLC from the Survival, Epidemiology, and End Results Program (SEER) database treated from 2004-2012 with either radiation alone or radiation followed by surgery. Potentially confounding variables which were extracted from the database included age, sex, race, and tumor location. The impact of patient and treatment variables on CSM and ACM was explored using Cox multivariable regression analysis - the potentially confounding factors listed above were included in the multivariable analysis.

Results: 14,065 patients were extracted from the SEER database. 42.2% of patients were age $<=64$, while 57.8% of patients were age >64. 39.7% of patients were female, while 60.3% were male. 79.0% of patients were white, 15.0% were black, and 6.0% were other. On multivariable analysis, even after adjustment for age, gender, race, and site, radiation followed by surgery was associated with a reduction in cause-specific mortality compared to radiation alone (adjusted HR = 0.46; 95% CI = 0.41, 0.52; $P<0.0001$). Median overall survival was 11 months in the radiation therapy alone arm versus 21 months in the radiation therapy plus surgery arm ($P<0.0001$ by log-rank test). After adjustment for these same factors, radiation followed by surgery was also associated with a reduction in all-cause mortality compared to radiation alone (adjusted HR = 0.47; 95% CI = 0.42, 0.52; $P<0.0001$). Median cause-specific survival was 12 months in the radiation therapy alone arm versus 33 months in the radiation therapy plus surgery arm ($P<0.0001$ by log-rank test).

Conclusion: In this population based analysis, there appears to be both a CSM and ACM benefit to adding surgery following radiation for Stage IIIB NSCLC. There are several limitations to this study including lack of chemotherapy data and the lack of data on medical co-morbidities. Indeed, our results are hypothesis generating, and would best be verified by a randomized clinical trial.

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Thoracic Radiation Therapy in Extensive-Stage Small Cell Lung Cancer: A Single-Institution Experience

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Purpose/Objective(s): The role of thoracic radiotherapy (TRT) in extensive stage small cell lung cancer (ES-SCLC) is unclear. There are data to support its use as consolidation following systemic therapy. The purpose of this retrospective review was to report outcomes of patients who received consolidative TRT (CTRT) at a single institution over 10 years.

Materials/Methods: Between January 2003 and December 2013, 457 patients received treatment for ESCLC at a single institution. Data were collected retrospectively from chart review and clinical registries using an institutional review board-approved database. Fifty-four patients received CTRT with a median dose of 45 Gy. The median number of fractions was 15. CTRT was delivered after a median 4 cycles of chemotherapy. CTRT was delivered concurrently with chemotherapy in 43% of cases. CTRT was delivered following clinical response to chemotherapy in 67% of cases, while the remainder had CTRT after no response, mixed response, or progression. Survival analyses were performed using Kaplan Meier analyses with SPSS version 22.

Results: Median follow-up was 21 months. For the entire cohort, receipt of CTRT was associated with an improved overall survival (OS) (17 vs. 7 months, $P < 0.001$). OS at 24 months was 33% vs. 7.5% for those receiving CTRT and not receiving CTRT, respectively ($P < 0.001$). Patients who received CTRT were less likely to have metastatic disease (M1). When adjusting for this imbalance, the improvement in overall survival persisted. In M1 patients, OS was 15 vs. 7 months ($P < 0.0001$), and in M0 patients, OS was 23 vs. 7 months ($P < 0.0001$). OS was 19 months and 15 months in those who received CTRT concurrent with chemotherapy and without concurrent chemotherapy, respectively ($P = 0.2$).

Conclusion: In this retrospective, single-institution series, CTRT was associated with superior survival. This finding persisted after adjusting for presence of distant metastases. Further study is warranted to elucidate the role of TRT in ES-SCLC.

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Risk Factors of Radiation Pneumonitis in the Patients With Non-Small Cell Lung Cancer Treated by Concomitant Chemoradiation Therapy: TOG/TROD Lung Cancer Study Group

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Purpose/Objective(s): To evaluate the clinical and DVH parameters that increase radiation pneumonitis in Turkish locally advanced NSCLC patients treated by concomitant chemoradiation therapy from nationwide multicentric data analyses.

Materials/Methods: Records of the 202/255 eligible patients from 7 different centers of Turkey were retrospectively reviewed. Age, gender, performance status, body weight, stage, tumor localization, tumor size, histology, chemotherapy scheme, smoking status, comorbid diseases, radiation therapy technique, and some DVH parameters (CTV, PTV, V5, V10, V20, and MLD) were reanalyzed. RTOG/EORTC pulmonary toxicity score was used for pneumonitis grading. X^2 test was performed for statistical analyses.

Results: Median follow-up was 13 months (5-77). Ninety percent of the patients were male and median age was 60 years (31-83). 14 patients were T1, 60 T2, 60 T3 and 66 were T4 tumor. 71% of the patients had epidermoid carcinoma. Platinum derives were used for the 65% of the patients. 127 patients were treated by conformal radiation therapy and 75 were irradiated by IMRT and the median radiation therapy dose was 61.2Gy (45-66.6). There were 69 patients with grade I, 69 patients with grade II, 14 patients with grade III, 1patient with grade IV and 1 grade V pneumonitis. Median time to pneumonitis after treatment was 3 months

(1-12). Cigarette smoking patients ($P=0.001$), patients treated with cisplatinum+etoposide ($P<.0001$), and patients whose irradiated MLD>16.5Gy ($P=0.002$), V10>45% ($P=0.003$) and V20>30% ($P=0.011$) had statistically more risk of radiation pneumonitis. The patients who had MLD>16.5Gy pneumonitis risk was increased by 3.3 times and V20>30%, it was increased by 3.6 times. No other factors were found to be a significant risk factor for pneumonitis.

Conclusion: In Turkish patients with NSCLC, we could not find relationship between any host-disease factor and pneumonitis risk except smoking. The most significant factors for radiation pneumonitis were found to be MLD>16.5Gy and V20>30%.

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Clinical Presentation and Distribution of Solitary Brain Metastases Among Non-Small Cell Lung Cancer (NSCLC) Patients in the Modern Staging Era

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Purpose/Objective(s): We sought to describe the clinical presentation and intracranial distribution of solitary brain metastases in NSCLC patients undergoing intracranial stereotactic radiosurgery (SRS) in the modern era of staging.

Materials/Methods: Through an IRB-approved retrospective review of departmental records, we identified 370 patients with NSCLC treated with intracranial SRS at our institution from 2001 and 2015. After screening all available radiographic and clinical records, 73 patients were found to have solitary brain metastasis based on staging body (70% PET-CT, 30% CT CAP +/- NM bone scan) and brain (95% MRI, 5% CT) scans.

Results: The median age at diagnosis of brain metastasis was 62 (range 41-87) years. 53% of patients were male and 47% were female. Median KPS was 80 (range 50-100). Median DS-GPA was 3.0 (range 2.0-4.0). Brain metastases were synchronous in 63% of cases and metachronous in 37% of cases. In metachronous patients, the median interval between diagnosis of NSCLC and diagnosis of brain metastasis was 15 (range 3-67) months. 85% of metachronous patients and 70% of synchronous patients were symptomatic at presentation of brain metastases; others were diagnosed by staging or follow up imaging. 25 patients (34%) underwent upfront craniotomy. Histology was most commonly adenocarcinoma (67%), followed by poorly differentiated NSCLC (15%), squamous cell carcinoma (11%), adenosquamous (3%), large cell (3%), and NSCLC NOS (1%). The most common location of solitary brain metastasis was frontal lobe (30%), followed by parietal lobe (27%), cerebellum (27%), occipital lobe (10%), temporal lobe (10%), and basal ganglia (2%). 52% of lesions were located on the right side and 47% were located on left side (1% midline). Median brain metastasis volume at diagnosis was 3.43 (range 0.03-47.71) cm^3. The thoracic stage was 28% T1, 25% T2, 25% T3, 21% T4 and 19% N0, 12% N1, 51% N2, 18% N3.

Conclusion: In a modern series of predominantly PET-CT and MRI staged NSCLC patients, most presented symptomatically with intracranial distribution of metastases proportional to relative anatomic volume.

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Cytokine Signature During Early Treatment May Predict Midtreatment Positron Emission Tomography/Computed Tomography and Survival in Non-Small Cell Lung Cancer

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Purpose/Objective(s): Imaging is a crucial part of oncologic practice, being involved in diagnosis, treatment planning, and follow-up. Active malignancy can result in a physiological environment which is reflected in PET-CT (FDG uptake and altered tissue density) and immune-inflammatory cytokine changes. Furthermore, radiation therapy has the potential to significantly impact these factors allowing them to serve as biomarkers both of tumor presence and treatment response. The goal of this study was to identify a correlation between PET-CT, cytokines, and survival in patients with non-small cell lung cancer.

Materials/Methods: Patients enrolled in prospective studies at 2 centers were eligible for analysis. Patients had blood collected pre-treatment (within 2 weeks before radiation therapy), during second week of treatment, and during fourth week of treatment for measurement of cytokines. 30 immuno-modulating and pro-inflammatory cytokines including IL1a, IL2, IL5, IL6, and TGFb1 were measured. Cytokine measurements were performed in platelet-poor plasma samples from the three time points using a commercial cytokine panel kit (multiplex assay for all but TGFb1 which used a molecule-specific enzyme-linked immunosorbent assay). All sample tests were run in duplicate. PET-CT was obtained pre-treatment and during treatment (at around 45Gy out of 60-86 Gy). Several imaging measurements were determined including SUV mean, SUV max, MTV, TLG, and CT GTV. Bayesian canonical correlation analysis (BCCA) was performed to generate PET-CT and cytokine signatures with a significant correlation. Correlation with survival was determined using Cox proportional hazards model.

Results: A total of 129 patients were included in this study. Using BCCA we generated signatures of both cytokine and PET-CT parameters. The PET-CT signature consisted of MTV, TLG, and CTGTV. The cytokine signature consisted of all cytokines. The signatures of baseline PET-CT and cytokine were correlated with each other significantly ($R=0.72$), but not correlated with overall survival (HR = 1.24, $P = 0.13$ and HR = 1.16, $P = 0.28$ respectively). Most interestingly, we have identified during treatment a PET-CT signature and second week during treatment a cytokine signature which strongly correlate with each other ($R^2 = 0.79$). Both of these PET-CT and cytokine signatures showed significant correlation with survival (HR = 1.31, $P = 0.003$ and HR = 1.24, $P = 0.046$ respectively).

Conclusion: This study has supported the potential of PET-CT and cytokine measurements to be used as biomarkers to predict survival. A cytokine signature based on measures taken during the second week of treatment may predict both future (fourth week during treatment) PET-CT response and survival, and has the potential to allow for improved adaptive planning.

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Patterns and Predictors of Failure Following Definitive Chemoradiation for Locally Advanced Non-Small Cell Lung Cancer (NSCLC)

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Purpose/Objective(s): Although definitive chemoradiation is the preferred treatment option for inoperable Stage III NSCLC, data regarding patterns of failure are limited. The objective of this analysis was to analyze patterns and predictors of disease recurrence in patients undergoing definitive chemoradiation for locally advanced non-small cell lung cancer.

Materials/Methods: We identified patients with stage III NSCLC undergoing definitive chemoradiation between 2005 and 2014 at a single institution. First failure sites were categorized as locoregional or distant. Kaplan-Meier method was used to assess time to treatment failure, and determine the cumulative incidence of locoregional or distant recurrence.