11.7%, with chest wall toxicity constituting 5.8% vs 8.6% and pneumonitis 5.8% vs 3.0%, respectively. For central versus non-central lesions, 5-year actuarial local control, distant metastases-free, disease failure-free, and overall survivals (in %) were 79.0 vs 75.4, 49.5 vs 56.7, 37.2 vs 34.3, and 18.3 vs 20.3, respectively. At analysis, crude rates by lesion of local, lobar and regional nodal failure (in %) were 11.2, 4.1 and 13.5, respectively. There were no statistically significant differences in the failure rates between central and non-central lesions for all parameters.

**Conclusions:** A decade’s experience with Lung SBRT using 50 Gy in 5 fractions reveals excellent local control. Patterns of cancer failure are mainly distant. Co-morbidities drive mortality in this population. This schedule is effective independent of tumor location in the lung, with minimal toxicities that are location-dependent.

**Author Disclosure:** G.M. Videtic: None. C. Reddy: None. N. Woody: None. T. Djemil: None. K. Stephens: None.

### 117 WITHDRAWN

### 118

**Stereotactic Body Radiation Therapy (SBRT) for Stage I Non-Small Cell Lung Cancer (NSCLC): Outcomes by Fractionation, Tumor Stage and Location, and Patient Operability**


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**Purpose/Objective(s):** SBRT is first-line therapy for medically inoperable stage I NSCLC. Limited data exist assessing SBRT outcomes by ability to undergo resection, tumor size and location, and fractionation. We hypothesized local control (LC) would be similar across fractionation regimens and in operable and inoperable patients (pts), overall survival (OS) would be higher for operable pts, and LC would be lower with increasing T stage.

**Materials/Methods:** All consecutive pts treated with SBRT at our institution from 6/2009-7/2013 for cT1-2aN0M0 stage I NSCLC were assessed in this IRB-approved study. Pts underwent CT or PET/CT scans as the earliest scan to show progression. Chi-square and Kaplan-Meier analysis were used for each endpoint.

**Results:** One hundred eighty-six pts with 204 lesions were analyzed. Pts were 50% male, 85% inoperable after thoracic surgeon evaluation, 68% white and had ECOG PS of 1 (59%) or 2 (26%). Lesions were adenocarcinoma (32%), squamous cell carcinoma (SCC, 24%) or suspicious on imaging but not histologically confirmed (37%). Pts were typically treated to 50 Gy in 4 (peripheral) or 5 (central) fractions. At 2 years, LC was 97%. LC did not differ by tumor location, fractionation or pt characteristics (all P>0.05) but tended lower for SCC (P = 0.06). LC was better for T1a-T1b than T2a (P = 0.05). Nodal and distant failure, cancer-specific survival (CSS) and OS did not differ by T stage (all P>0.05). Overall, 21% had locoregional failure. Operable pts refusing surgery had similar LC (100% vs 96%, P = 0.28), nodal (7% vs 14%, P = 0.33) and distant (7% vs 4%, P = 0.45) failure, and CSS (96% vs 96%, P = 0.86), although they tended to worse 2-year (85% vs 69%, P = 0.09) and median (not reached vs 34 months, P = 0.12) OS than inoperable pts. Outcomes were similar with or without pathologic confirmation (LC P = 0.64, OS P = 0.43). Grade 2 rib fracture occurred in 1%, chest wall syndrome 6% and pneumonitis 3%. Lung mean dose (P = 0.06) and V20 (P = 0.08) trended toward pneumonitis association. No grade ≥2 acute or late toxicity was observed.

**Conclusions:** This study showed SBRT is well tolerated and can achieve high LC. LC was less for tumors >3 cm but did not differ by tumor location or fractionation, likely since all regimens were BED >100. Nodal and distant failures were limited, likely due to pre-SBRT universal PET/CT staging and often pathologic nodal staging. Although LC and CSS were similar for operable and inoperable pts, inoperable pts had somewhat lower OS, likely due to greater comorbidities. Mature prospective data from RTOG 0618 and JCOG 0403 are needed to better assess SBRT in operable pts.


### 119 WITHDRAWN

### 120

**Reurrence Patterns and Second Primary Lung Cancers After Stereotactic Body Radiation Therapy for Early-Stage Non-Small Cell Lung Cancer: Implications for Surveillance**

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**Purpose/Objective(s):** Similar to surgically resected patients with early-stage non-small cell lung cancer (NSCLC), patients treated with stereotactic body radiation therapy (SBRT) most commonly fail in intrathoracic lymph nodes, distant sites or develop second primary lung cancers. The optimal surveillance regimen remains unclear. We investigated the post-treatment recurrence patterns and development of second primary lung cancers (SPLC) to identify the most critical time periods after definitive SBRT.

**Materials/Methods:** We identified 368 patients who received SBRT (median radiation dose: 4800 cGy in 4 fractions) for inoperable early-stage NSCLC at our institution between 2006 and 2013. Patients typically underwent a CT scan of the chest every 3 months during years 1 and 2, every 6 months during years 3 and 4, and annually thereafter. Competing risks analysis was used for local (LFFS), nodal (NFFS) and distant failure-free survival (DFFS) and the cumulative incidence of SPLC. SPLC were defined as new primary lung cancers when occurring in a different lobe or lung or a different histology or subtype. Kaplan-Meier analysis was used to estimate overall survival (OS). Candidate factors on univariate analysis (UVA) were incorporated into a multivariate model (MVA) for each endpoint.

**Results:** The majority of patients (n = 299; 81%) had T1 tumors, and 258 (70%) had an adenocarcinoma. Thirty-seven (10%) were never smokers, 292 (79%) former smokers, and 39 (11%) current smokers. With a median follow up of 24 months, the 2-year cumulative incidence of local, nodal, and distant failure was 12.5%, 16.0%, and 15.4%. The 2-year OS was 67.5%. In 96 out of 109 patients (88%) with disease progression, this occurred within the first 2 years after SBRT. Six patients progressed in the third year, and seven thereafter. On MVA, adenocarcinoma histology and tumor size ≤2 cm were the most significant factors for favorable LFFS; tumor size for DFFS; and younger age, KPS >80, adenocarcinoma histology, and tumor size for OS. None of these factors correlated with NFFS. Nineteen patients (5%) developed a SPLC, with a median time to development of SPLC of 16.5 months (range 6.5 to 71.1 months). The cumulative incidence of SPLC continued to rise up to 6 years from the end of SBRT, with 6 patients developing SPLCs after 2 years. None of the never smokers, but 13 (4%) former and 6 (15%) current smokers developed a SPLC (P = 0.005).

**Conclusions:** Close monitoring with chest CT scans within the first 2 years after SBRT is effective in detecting early disease progression. In contrast,
the risk for developing a SPLC remains elevated beyond 2 years, particularly in former and current smokers. Therefore, continued surveillance beyond 2 years should be maintained.


Predictors of 30-Day Mortality Following Resection of Early-Stage NSCLC: An Analysis of the National Cancer Data Base
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Purpose/Objective(s): Studies examining morbidity after lobectomy for early stage NSCLC have shown that patients over the age of 65 have a > 50% incidence of complications, and this risk increases significantly in elderly patients (age ≥ 75). Factors that affect postsurgical 30-day mortality (30-DM), however, are less well defined.

Materials/Methods: The National Cancer Data Base (NCDB), was used to identify patients 19 years and older with a diagnosis of stage I NSCLC (cT1-2, cN0, cM0) between the years 2003 and 2011. Data from patients who underwent surgical resection with lobectomy or sublobar resection were abstracted. Univariate and multivariate analysis was performed for predictors of 30-DM. Factors examined included: age, sex, year of diagnosis, tumor size, and Charlson-Deyo (CD) morbidity score.

Results: A total of 112,216 patients met the criteria. Of these, 71,175 or 64% received surgery, and of this group, 57,569 (81%) underwent lobectomy and 13,606 (19%) underwent sublobar resection. Pneumonectomy patients were excluded. The median age was 68 years (53% female). Median tumor size (Tsize) was 2.4 cm. CD score was 0 in 49% of patients and 1 or higher in 51%. The overall rate of 30-DM was 2.2%. On univariate analysis, younger age, treatment at a research/academic institution, female sex, Tsize ≤ 3 cm, and Charlson-Deyo (CD) score of 0 were protective against 30-day mortality, while treatment at a community cancer center predicted for worse 30-DM. Extent of surgery was not significant. On multivariate analysis, younger age, CD score of 0, female sex, Tsize ≤ 3 cm, and treatment at a comprehensive community cancer center or an academic/research center were protective against 30-DM (P < .001 for all). While the overall 30-DM rate was low, an interesting picture emerged when age and comorbidity were examined together (Table). In patients younger than 75 years with medical comorbidities, the 30-DM was 1.8%. However, in elderly patients with comorbidities this rate nearly tripled to 4.6% (P < .001). Much of this difference was driven by elderly patients with comorbidities who underwent lobectomy, in whom the 30-DM climbed to 5.1% as opposed to 3.1% with sublobar resection (P < .001).

Conclusions: The overall 30-DM rate following sublobar or lobar resection was quite low. In patients older than 75 years with medical comorbidities, however, this incidence nearly triples; suggesting improved perioperative care, consideration of more limited resection, or consideration of effective nonsurgical therapies may be indicated.


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<th>Thoracic Abstract 121: Table</th>
<th>30-DM as a function of age, CD comorbidity score, and type of surgery</th>
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<td>Age</td>
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<td>CD 0</td>
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Note: €, ¥, * all represent significant comparisons with P < .05

Predictive Significance of Actinin-4 (ACTN4) Gene Expression in Early-Stage Non-Small Cell Lung Cancer (NSCLC)
T. Yamada and K. Honda; National Cancer Center Research Institute, Tokyo, Japan

Purpose/Objective(s): Even if detected at an early stage, a significant proportion of NSCLCs relapse after curative surgery. Postoperative adjuvant chemotherapy is expected to improve overall outcome. However, as the majority of early-stage NSCLCs do not relapse, only high-risk patients accounting for a small proportion of the total actually benefit from such treatment. In fact, a retrospective subset analysis of stage IB patients in the CALGB 9633 trial revealed that only individuals with a tumor diameter of http://www.practicalradonc.org/content/podcast 4 cm obtained a survival benefit from adjuvant chemotherapy. Amplification of the ACTN4 cell motility gene was recently shown to be associated with an extremely high risk of postsurgical death [hazard ratio (HR) = 10.53] in patients with stage I lung adenocarcinoma. Therefore we investigated whether expression of ACTN4 was able to predict whether adjuvant vinorelbine and cisplatin would be of benefit to patients with stage-IB and -II NSCLC who were enrolled in the NCIC CTG JBR.10 randomized trial.

Materials/Methods: Sixty-two patients in the control arm (observation alone) were divided into those showing high and low expression of the ACTN4 gene using the X-tile algorithm. The same cut-off value was applied to 71 patients who received adjuvant chemotherapy.

Results: One hundred eight patients whose tumors showed a low level of ACTN4 expression did not obtain any significant survival benefit from the adjuvant therapy [HR = 1.01 (95% CI: 0.57-1.77), P = .979], whereas a clear benefit was evident in 25 patients whose tumors showed a high level of ACTN4 expression [HR = 0.27 (95% CI: 0.08-0.95), P = .030]. Cox regression analysis confirmed that ACTN4 gene expression was predictive of the response to adjuvant therapy (Interaction P = .048).

Conclusions: Various multi-gene expression signatures have been generated from microarray data, but their prognostic significance has not always been reproducible among different patient cohorts. Amplification of a single gene, ACTN4, clearly defines a small subset of high-risk patients with stage I lung adenocarcinoma. The prognostic significance of ACTN4 has been reproducibly observed in 3 independent cohorts totaling 1033 patients and exceeds that of conventional TNM staging. The roles of ACTN4 in cancer invasion and metastasis have been well demonstrated in various animals. We conclude that ACTN4 expression has the potential to discriminate patients with early-stage NSCLC who would benefit from adjuvant chemotherapy.

Author Disclosure: T. Yamada: None. K. Honda: None.

Phase 2 Trial of Preoperative Pemetrexed (P)/Carboplatin (C) in Patients (Pts) With Select Stage IB, II, and III Nonsquamous Non-Small Cell Lung Cancer (NS-NSCLC)
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Purpose/Objective(s): Adjuvant chemotherapy is standard treatment (tx) for operable NSCLC. Potential advantages of preoperative tx include earlier tx of micrometastases and better tx tolerance. Adjuvant P/Cisplatin was less toxic and easier to deliver than vinorelbine/cisplatin. This is a phase 2 trial of preoperative P/C in pts with nonsquamous stage I-III NS-NSCLC.

Author Disclosure: R.B. Mitchell,8 H.A. Burris,1,2 J.D. Hainsworth,1,2 and F.A. Greco1,2; Ft. Myers, FL, 6Medical Oncology Associates of Augusta, Augusta, GA, 1Sarah Cannon Research Institute; Nashville, TN, 2Tennessee Oncology, Nashville, TN, 3Ohio Hematology Care, Cincinnati, OH, 4Center for Cancer and Blood Disorders, Bethesda, MD, 5Florida Cancer Specialists, Ft. Myers, FL, 6Medical Oncology Associates of Augusta, Augusta, GA, 7South Carolina Oncology Associates, Columbia, SC, 8Virginia Cancer Institute, Richmond, VA.