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HILTON SAN DIEGO BAYFRONT | SAN DIEGO | MARCH 14-16, 2019

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2019 Thoracic Cancers Symposium Abstracts

PLENARY SESSION

1

Improved Overall Survival with Local Consolidative Therapy in Oligometastatic Non-Small Cell Lung Cancer: Results from a Cohort of 194 Patients with Synchronous Disease

K.G. Mitchell,¹ A. Farooqi,² E.B. Ludmir,² E.M. Corsini,¹ A.A. Vaporciyan,¹ S.G. Swisher,¹ J. Heymach,³ J. Zhang,³ D.R. Gomez,² and M. Antonoff¹; ¹Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, ²Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, ³Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Purpose/Objective(s): Treatment strategies consisting of aggressive local therapy represent an evolving paradigm for select patients with advanced non-small cell lung cancer (NSCLC) who present with a limited burden of metastatic disease. We hypothesized that local consolidative therapy (LCT) to the primary lesion and metastatic foci would be associated with improved overall survival (OS) among patients with synchronous oligometastatic NSCLC.

Materials/Methods: Patients presenting to a single institution (2000-2017) with stage IV NSCLC and ≤ 3 synchronous metastatic lesions were identified. Intrathoracic nodal disease was counted as one site. Univariable and multivariable Cox regressions were performed to identify factors associated with overall survival. A ninety-day landmark analysis was performed to limit survivorship bias.

Results: Of 194 patients (median age 62 years; male 111 [57%]), 146 (75%) had adenocarcinoma. 136 (70%) had 2-3 sites of non-regional metastasis, with 86 (44%) brain, 51 (26%) bone, and 36 (19%) adrenal as the most common sites of distant disease. Systemic therapy was administered in 175 (90%). LCT to the primary lesion was used in 145 (75%), to all distant metastases in 147 (76%), and to all disease sites in 121 (62%). Rates of locoregional progression were lower in patients who received LCT to the primary tumor (30/145, 21%) than those who did not (21/49, 43%) ($p < 0.01$). After a median follow-up of 52.3 (IQR 29.9-98.0) months, median OS for the cohort was 26.5 (CI 23.0-30.0) months. Though the site of metastatic disease was not associated with prognosis on univariable analysis, progression on first-line systemic therapy was associated with an increased hazard of death (HR 1.87, CI 1.15-3.02, $p = 0.01$). Comprehensive LCT to all sites of disease was associated with improved OS (HR 0.67, CI 0.47-0.96, $p = 0.03$); a similar trend toward improved survival was observed with receipt of LCT to the primary lesion (HR 0.71, CI 0.49-1.05, $p = 0.08$). In contrast, LCT to distant metastases was not associated with a survival benefit (HR 0.77, CI 0.52-1.16, $p = 0.21$). On multivariable analysis, receipt of comprehensive LCT to all sites of disease (HR 0.68, CI 0.47-0.97 $p = 0.032$) and adenocarcinoma histology (HR 0.71, CI 0.56-0.90, $p = 0.004$) remained independently associated with improved OS.

Conclusion: Aggressive consolidative therapy to the primary lesion and all metastatic sites was associated with improved overall survival in this large, retrospective series of patients with synchronous oligometastatic NSCLC. These results support ongoing prospective efforts to fully characterize the therapeutic benefits associated with this management strategy.

Author Disclosure: K.G. Mitchell: None. A. Farooqi: None. E.B. Ludmir: None. E.M. Corsini: None. A.A. Vaporciyan: None. S.G.

Swisher: Consultant; GlaxoSmithKline. J. Heymach: None. J. Zhang: None. D.R. Gomez: Research Grant; Merck, AstraZeneca. Honoraria; BMS. Speaker's Bureau; Merck, Varian. Advisory Board; AstraZeneca. M. Antonoff: None.

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Upstaging in Repeat PET/CT prior to Chemoradiation in Locally Advanced NSCLC: Implications for Clinical Care

J. Zeng,¹ B. Sasidharan,¹ R. Rengan,¹ H.M.T. Thomas,¹ and S.R. Bowen²; ¹University of Washington, Department of Radiation Oncology, Seattle, WA, ²University of Washington, Department of Radiation Oncology & Radiology, Seattle, WA

Purpose/Objective(s): Accurate staging of patients newly diagnosed with lung cancer is crucial to selecting the most appropriate treatment regimen. As healthcare costs continue to rise, more restrictions are placed on imaging studies including frequency of repeat scans that are allowed. This can lead to under-staging patients with relatively advanced and aggressive malignancies, including stage III non-small cell lung cancer (NSCLC). We present the longitudinal staging dynamics of patients enrolled on the Functional Lung Avoidance & Response-adaptive Escalation (FLARE-RT) phase II trial who had repeat PET/CT within two months of an initial diagnostic PET/CT.

Materials/Methods: Twenty stage IIB-IIIb NSCLC patients planned for definitive chemoradiation underwent a repeat PET/CT paid for by research funds as part of the FLARE-RT trial, which requires a PET/CT within one month of starting radiation, to be performed on our institutional scanners. All 20 patients had an initial PET/CT performed for staging. Changes in T-stage, N-stage, and M-stage were recorded. PET/CT tumor characteristics were recorded including metabolic tumor volume (MTV), SUVmax, SUV mean, SUVpeak, and total lesion glycolysis (TLG). Patients who were upstaged were compared against patients not upstaged with non-parametric testing using Kruskal-Wallis ANOVA.

Results: Median days between initial and repeat PET/CT was 35 days (range 15-63). Two out of 20 patients (10%) were found to have metastatic disease on repeat PET/CT and underwent systemic therapy instead of chemoradiation. An additional five patients (25%) were upstaged to N3 disease on repeat PET/CT from N2 disease on initial scan, which led to significant changes in their radiation fields. No T-stage changes led to upstaging. Comparing patients who were upstaged on repeat PET/CT versus patients who were not, no statistically significant difference was found in terms of number of days between the two scans, MTV, TLG, SUVmax, SUVmean, and SUVpeak (Table 1).

Conclusion: For patients with locally advanced NSCLC planned for definitive chemoradiation, a repeat PET/CT performed at a median of 35 days after an initial scan leads to 10% of patients being upstaged to stage 4 disease, where upfront radiation treatment is no longer appropriate. An additional 25% of patients had significant changes in nodal staging and treatment volume. Current practice guidelines as well as insurance coverage policy should consider the cost-effectiveness of short-term repeat staging scans.

Author Disclosure: J. Zeng: None. B. Sasidharan: None. R. Rengan: Consultant; Astra-Zeneca. Travel Expenses; IBA. H.M. Thomas: None. S.R. Bowen: Research Grant; National Cancer Institute.

Table 1 Comparison of patients upstaged on repeat PET/CT versus patients not upstaged.

	Number of Patients	Median Days Between Scans	Median SUVmax	Median SUVmean	Median SUVpeak	Median MTV (ml)	Median TLG (SUV ml)
All Patients	20	35	11	6	9	36	283
Patients Upstaged	7	34	13	8	13	115	883
Patients Not-Upstaged	13	36	11	6	9	35	201

3

The Impact of the Stage III Randomized Trial by Takahashi et al. on the Use of Prophylactic Cranial Irradiation (PCI) in Patients with Extensive-Stage Small-Cell Lung Cancer (ES-SCLC)



O. Gjyshi,¹ E.B. Ludmir,² A. Dursteler,³ and S.H. Lin⁴; ¹MD Anderson Cancer Center, Houston, TX, ²University of Texas MD Anderson Cancer Center, Houston, TX, ³The University of Texas MD Anderson Cancer Center, Houston, TX, ⁴Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Purpose/Objective(s): While controversial, the EORTC phase III PCI trial in ES-SCLC (Slotman *et al.*, NEJM 2007) demonstrated an overall survival (OS) advantage of PCI. This drastically altered the practice pattern in the US such that most radiation oncologists had come to accept the practice of PCI as standard of care for ES-SCLC patients. Recently, however, Takahashi *et al.*, (NEJM 2017) reported a contemporary phase III clinical trial that demonstrated no OS advantage of PCI when compared to observation with close MRI surveillance, although it did reduce the incidence of intracranial metastases. The impact of this recent trial on clinical practice in the US is unknown.

Materials/Methods: Over a two-week period in September 2018, a total of 205 attending radiation oncologists who specialize in the treatment of thoracic malignancies from 105 academic centers in the US were contacted via email to participate in an anonymous 24-question survey regarding the use of PCI in ES-SCLC pre- and post-publication of the Takahashi *et al.* study.

Results: A total of 49 (24%) radiation oncologists responded to the survey. Responders were evenly distributed geographically within the US. The majority of the responders were from large academic centers (>10 radiation oncologists) (67%), and 42% of them had lung cancer cases constitute >50% of their practices. All respondents were aware of the Takahashi *et al.* trial. While 78% routinely offered PCI for ES-SCLC prior to the publication, only 38% of them continued to do so after its publication ($p < 0.01$, Fisher's exact test). A majority of respondents (67%) had altered their practice patterns in response to the Takahashi, *et al.* trial. Subset analyses showed no significant trends in post-Takahashi PCI usage pattern based on physicians' geographic location, years of practice or volume of SCLC cases treated (all $p > 0.1$). Individual responder comments indicate that close MRI surveillance is often being utilized as an alternative to PCI and that medical oncologists had significantly reduced referrals in this patient population since the publication of Takahashi *et al.*

Conclusion: The study by Takahashi *et al.* has markedly impacted current practice patterns in the US by reducing PCI use for ES-SCLC among academic radiation oncologists. We observed a decrease in PCI utilization for ES-SCLC from 78% to 38% following publication of this trial. The lack of equipoise in practice approaches and a reduction in clinical referral may negatively impact physician participation in similar randomized clinical trials regarding PCI being planned in the US and Europe.

Author Disclosure: O. Gjyshi: None. E.B. Ludmir: None. A. Dursteler: None. S.H. Lin: Research Grant; STCube Pharmaceuticals, Inc, Roche/Genentech, Hitachi Chemical, Inc, New River Labs, Beyond Spring Pharmaceuticals, Inc. Advisory Board; AstraZeneca Inc.

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Tumor Treating Fields plus chemotherapy for first-line treatment of malignant pleural mesothelioma: Final Results of the STELLAR Trial



G. Ceresoli,¹ J. Aerts,² J. Madrzak,³ R. Dziadziuszko,³ R. Ramlau,⁴ S. Cedres,⁵ B. Hiddinga,⁶ J.P. Van Meerbeeck,⁶ M. Mencoboni,⁷ D. Planchard,⁸ A. Chella,⁹ M. Krzakowski,¹⁰ L. Crino,¹¹ and F. Grosso¹²; ¹Istituto Clinico Humanitas IRCCS, Rozzano (MI), Italy, ²Erasmus MC, Rotterdam, Netherlands, ³Medical University of Gdansk Clinical Hospital, Gdansk, Poland, ⁴Poznan University of Medical Science, Poznan, Poland, ⁵Vall d'Hebron University Hospital, Barcelona, Spain, ⁶University Hospital Antwerp, Antwerp, Belgium, ⁷Villa Scassi Hospital, Genova, Italy, ⁸Gustave Roussy, Villejuif, France, ⁹Department of Thoracic Surgery, University of Pisa, Pisa, Italy, ¹⁰Maria Sklodowska Curie Memorial Cancer Centre in Warsaw, Warsaw, Poland, ¹¹Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori – IRCCS, Meldola, Italy, ¹²SS Antonio e Biagio Hospital, Alessandria, Italy

Purpose/Objective(s): Tumor Treating Fields (TTFields) are an anti-mitotic, regional treatment comprising low-intensity, intermediate frequency, alternating electric fields delivered non-invasively to the tumor by a portable medical device. TTFields plus chemotherapy significantly extended survival of glioblastoma patients. Human mesothelioma cells are susceptible to TTFields in vitro. The Phase 2 STELLAR (NCT02397928) trial studied the efficacy and safety of TTFields concomitant with pemetrexed plus platinum (cisplatin or carboplatin) in malignant pleural mesothelioma (MPM) versus historical data (Vogelzang *et al.* JCO 2003).

Materials/Methods: Eighty patients with unresectable, previously untreated MPM were treated with continuous 150 kHz TTFields (≥ 18 h/day) plus standard dosing of pemetrexed with either cisplatin or carboplatin. Inclusion criteria: ECOG PS of 0-1, pathologically proven MPM and ≥ 1 measurable lesion per modified RECIST. Patients were followed q3w (CT scan q6w) till disease progression. The primary endpoint was overall survival (OS). Secondary endpoints were response rate, progression free survival (PFS) and toxicity. Assuming historical control data with a median survival of 12.1 months, the sample size ($N=80$) provides 80% power with a two-sided alpha of 0.05 to detect an increase in median OS of 5.5 months.

Results: Patients enrolled from 2016 to 2017 were median age was 67 (range 27-78), 84% males, 56% smokers, 16% (13 patients) had metastatic disease, 44% (35 patients) had ECOG PS 1, and 66% (53 patients) had epithelioid histology. TTFields median compliance was 68% (12 hours/day). 63% (50 patients) received carboplatin. Median OS was 18.2 months (95% CI 12.1-25.8) compared to 12.1 months in the historical control. Median OS in epithelioid patients was 21.2 months (95% CI 13.2-25.8). Median PFS was 7.6 months (95% CI 6.7-8.6) versus 5.7 months in the historical control. Partial response was 40.3% and disease control rate (PR+SD) was 97.2%. No device-related serious adverse events (AEs) were reported. TTFields-related dermatitis was reported in 46% (37 patients). Four patients (5%) had grade 3 dermatitis, which resolved after corticosteroid treatment or treatment break. Grade 3-4 AEs were reported in 26% of patients.

Conclusion: TTFields plus pemetrexed and a platinum agent were effective and safe for the treatment of unresectable MPM. Median OS (18.2 months) was longer than the historical control (12.1 months). Despite the lower rate of patients with epithelioid histology, OS was better than the

metemred/platinum arm in recent trials (MAPS, LUME-Meso). There was no increase in systemic toxicity with TTFields. The only TTFields-related adverse event was skin irritation beneath the transducer arrays.

Author Disclosure: G. Ceresoli: Travel Expenses; Novocure. J. Aerts: None. J. Madrzak: None. R. Dziadziuszko: None. R. Ramlau: None. S. Cedres: None. B. Hiddinga: None. J.P. Van Meerbeek: None. M. Mencoboni: None. D. Planchard: None. A. Chella: None. M. Krzakowski: None. L. Crino: None. F. Grosso: None.

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The Impact of Structured, Prospective Exposure to the NCCN Guidelines when Making Treatment Decisions: Improved Metrics of Guideline-Concordant Care for Patients with Non-Small Cell Lung Cancer



S.Y. Wu,¹ A. Lazar,¹ M.A. Gubens,¹ C.M. Blakely,¹ A.R. Gottschalk,¹ A.A. Garsa, Jr.,² D. Jablons,¹ T.M. Jahan,¹ V.E.H. Wang,¹ T. Dunbar,¹ R. Paz,¹ L. Curran,¹ W. Guthrie,³ J. Belkora,¹ and S.S. Yom¹; ¹University of California, San Francisco, San Francisco, CA, ²University of Southern California, Los Angeles, CA, ³Patients with Power, San Francisco, CA

Purpose/Objective(s): A structured, interactive web-based tool was designed to present the NCCN guidelines to non-small cell lung cancer (NSCLC) patients, tailored to their individual clinical and pathologic features. We evaluated differences in guideline concordance according to 6 metrics assessed before and after implementation of the tool.

Materials/Methods: This was an IRB-approved, prospective clinical trial assessing feasibility, acceptability, and clinical impact. We enrolled 76 patients with NSCLC, newly diagnosed or at the time of new disease progression. Patients were introduced to the web-based tool by a trained coordinator and were assisted in accessing it during and after their initial consultation. Guideline concordance was evaluated in a binary (yes/no) fashion for 6 metrics: 1) smoking cessation/intervention; 2) adjuvant chemotherapy for stage IB-IIB patients undergoing surgery; pathologic mediastinal staging in stage III patients prior to 3) surgery or 4) nonsurgical treatment; 5) upfront definitive chemoradiation for stage III patients; and 6) molecular testing for EGFR and ALK mutations prior to systemic therapy for stage IV disease. Baseline level of guideline concordance was evaluated in a series of 159 patients seen before the tool was available and results were compared to concordance when the tool was available.

Results: Median age at the time of study was 67.5 years (interquartile range, 14 years). The most common histologies were adenocarcinoma and squamous cell carcinoma in the study group (78% and 18%, respectively) and the retrospective cohort (67%, 18%) ($p = 0.10$). Among patients exposed to the tool, there was an increase in smoking cessation counseling/intervention in active smokers (80% vs. 4%, $p < 0.001$). There was a decrease in use of adjuvant chemotherapy following surgery for stage IB-IIB disease (0/8 (0%) vs. 6/12 (50%), $p = 0.02$). This decrease was mostly driven by decreased use of adjuvant chemotherapy for stage IB NSCLC resected with negative margins (0/6 vs. 4/4 in the comparison group, $p = 0.04$). There was an increase in molecular testing prior to initiation of systemic therapy in patients with metastatic NSCLC experiencing the tool (96% vs. 68%, $p = 0.01$). In patients with stage III NSCLC, there were no differences in the frequency of pathologic mediastinal staging performed prior to surgery ($p = 0.70$) or nonsurgical treatment ($p = 0.55$). Likewise, the use of upfront chemoradiation in non-operative candidates was not different between study patients and the comparator cohort ($p = 0.55$).

Conclusion: Structured exposure to the NCCN guidelines during and after oncology consultation improved guideline concordance in smoking cessation, testing for molecular markers, and more judicious use of adjuvant chemotherapy. These findings add further support that evidence-based decision and communication aids can improve cancer care.

Author Disclosure: S.Y. Wu: Employee; Stanford. A. Lazar: None. M.A. Gubens: Consultant; AstraZeneca, Bristol Myers Squibb, Genentech/Roche, Novartis, Mersana. C.M. Blakely: Research Grant; Novartis, Clovis, Mirati, Igntya, Medimmune, AstraZeneca. Consultant; Jazz

pharmaceutical. A.R. Gottschalk: Employee; University of California. A.A. Garsa: Partner; CHLA. D. Jablons: Stock; Encore Clinical. T.M. Jahan: Speaker's Bureau; Novartis. V.E. Wang: None. T. Dunbar: None. R. Paz: None. L. Curran: None. W. Guthrie: None. J. Belkora: Unpaid; Cancer Support Community. S.S. Yom: Research Grant; Genentech, Merck, Bristol-Myers Squibb. Royalty; UpToDate, Springer. Honoraria; ASTRO; Am Radium Society-Am College of Radiology, American Society for Radiation Oncology, American Radium Society.

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Multidisciplinary Treatment of Thymic Neuroendocrine Tumors: Evaluation of the Impact of Surgery, Chemotherapy, and Radiation



E.M. Corsini, K.G. Mitchell, R. Mehran, D.C. Rice, B. Sepesi, G. Walsh, S.G. Swisher, J. Roth, A.A. Vaporciyan, W. Hofstetter, and M. Antonoff; Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX

Purpose/Objective(s): Thymic neuroendocrine tumors (TNET) are rare malignancies often treated in a multidisciplinary fashion. However, evidence for adjunctive therapy is limited, and predictors of survival and recurrence are not well established. Therefore, we reviewed our experience with TNET to determine best treatment practices and predictors of survival.

Materials/Methods: Patients treated for TNET at a single center from 1975 to 2018 were reviewed. Variables collected pertained to tumor factors, stage, and treatments, including surgery. Univariate and multivariate regression analyses were used to determine predictors of overall survival (OS) and recurrence.

Results: We identified 49 patients treated for TNET, among whom 36 (74%) were male with a median age of 46 years (IQR 38-54) (Table). Metastatic disease was present in 9 (18%), and 11 (22%) had MEN1. Surgical resection was not undertaken in 8 (16%) patients, 4 (50%) of whom had metastases, who instead received chemotherapy and radiation in 7 (88%) and 2 (25%) cases, respectively. Locally invasive and positive nodes were found in 19 (46%) cases each upon resection. Recurrence following surgery was seen in 29 (71%) patients, including 21 (51%) with intrathoracic recurrence. After a median follow up of 57.4 months, median and recurrence free survival were 80.4 and 24.5 months, respectively. The 5-year survival (5YS) for those who did and did not undergo resection were 62% versus 21% ($p = 0.002$). For those with and without metastases, the 5YS was 48% versus 56%, respectively ($p = 0.149$). Age, induction chemotherapy, and metastases, predicted OS in univariate analysis. In multivariate analysis, induction chemotherapy increased hazard of death ($p = 0.019$; HR 3.62; CI₉₅ 1.23-10.63). Tumor size predicted intrathoracic recurrence in multivariate analysis ($p = 0.006$; HR 1.24; CI₉₅ 1.06-1.44).

Conclusion: Our data, representing the largest single center experience with TNET, suggest surgery is important to OS, while there is unclear evidence for the benefit of adjunctive therapies. Additionally, it is likely that those receiving induction chemotherapy represent a unique cohort with advanced or aggressive disease. Among surgical candidates, tumor size predicts intrathoracic recurrence.

Univariate Analysis for Survival in those Undergoing Surgical Resection.

Variable	n (%)	HR	95% CI	p Value
Age		1.02	0.99 – 1.06	0.245
Induction chemotherapy (yes)	9 (22)	3.12	1.10 – 8.82	0.032
Induction radiation (yes)	1 (2)	0.79	0.10 – 5.97	0.815
Adjuvant chemotherapy (yes)	13 (32)	1.25	0.53 – 2.93	0.613
Adjuvant radiation (yes)	18 (44)	1.30	0.56 – 3.01	0.540
Adjuvant bimodality therapy (yes)	8 (20)	1.03	0.40 – 2.66	0.954
Tumor size, cm		1.06	0.90 – 1.24	0.512
Positive margins	13 (32)	1.22	0.50 – 2.98	0.656
Metastases (yes)	5 (12)	2.42	0.68 – 8.60	0.173

Univariate Analysis for Survival in those Undergoing Surgical Resection:

Author Disclosure: E.M. Corsini: None. K.G. Mitchell: None. R. Mehran: None. D.C. Rice: None. B. Sepesi: None. G. Walsh: None. S.G. Swisher: None. J. Roth: None. A.A. Vaporciyan: None. W. Hofstetter: None. M. Antonoff: None.

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Correlation of Survival Outcomes with Clinical and Molecular features in Lung Cancer Patients Treated with Immune Checkpoint Inhibitors



R. Chen, A.G. Azzouqa, Y. Zhang, J.A. Marin-Acevedo, R. Manochakian, and Y. Lou; *Mayo Clinic Florida, Jacksonville, FL*

Purpose/Objective(s): Immune checkpoint inhibitors (ICIs) have become standard of care for non-small cell lung cancer (NSCLC) and have showed benefit in small cell lung cancer as well. However, some patients fail to respond to ICIs despite high PD-L1 tumor proportion score (TPS) and/or Tumor mutation burden (TMB). There is an unmet need to identify patients who will benefit from ICIs. We investigated the efficacy and safety of ICIs in the real world and alternative predictive factors for survival in patients with advanced lung cancers.

Materials/Methods: We performed an observational study to evaluate the activity of ICIs in lung cancer patients in a single institution. All lung cancer patients who started treatment with ICIs from March 2015 to December 2017 were included. ICIs included nivolumab, pembrolizumab, atezolizumab as single agents, ipilimumab/Nivolumab or Pembrolizumab/chemotherapy combinations. Progression-free survival (PFS) was computed from date of initiation of ICIs. Analyses were performed by SAS software 9.4. Kaplan-Meier Log-Rank test was used for survival statistical analysis.

Results: Out of 120 patients who received ICIs, 57(47.5%) were females and 63 (52.5%) were males; median age was 71(range 45-92); 89(74.2%) had adenocarcinoma, 28(23.3%) squamous, and 3 (2.5%) small cell carcinoma. Most patients (69.2%) had received prior systemic therapy and 46.7% had received prior radiation. An objective response was recorded in 14.1% (17/120) patients including one complete response. Thirty-four patients (28.3%) achieved stable disease (SD). Median TMB was 9 in responders and 8 in non-responders. Median PFS in patients with SD or better was 425 days compared to 66 days in non-responders ($P<0.0001$). PD-L1 status was tested in 67 patients: 27(40.3%) had $>50\%$, 14 (20.9%) had 1-49%, and 26(38.8%) had $<1\%$ and PFS was 151 days/Not reach/81 days, respectively but there was no statistical difference. Grade 1-3 immune-related adverse events (IrAEs) occurred in 20.8% (25/120) patients and 9.2% (11/120) required systemic corticosteroids. Eighty-four patients had Next-generation sequencing (NGS) data. NF1 and CD79a were identified in 7.1-9.5% of patients and correlated with worse PFS. AKT3 was found in 11.9% of 84 patients who demonstrated a trend towards a better PFS.

Conclusion: Although further validation is required, molecular profiling with NF1, CD97a, and AKT3 could potentially enrich the predictive

values for survival in lung cancer patients receiving Immune checkpoint inhibitors.

Author Disclosure: R. Chen: Employee; GlaxoSmithKline. Stock; Eli Lilly and company, GlaxoSmithKline. A. Azzouqa: None. Y. Zhang: None. J.A. Marin-Acevedo: None. R. Manochakian: Advisor; Takeda. Y. Lou: None.

ORAL ABSTRACT SESSION

8

Stereotactic Ablative Radiotherapy (SABR) in Early Stage Non-Small Cell Lung Cancer: A National Cancer Database (NCDB) Propensity Matched Analysis Comparing Survival in Adenocarcinoma and Squamous Cell Carcinoma



S. Abel,¹ S. Hasan,² R. White,³ L. Schumacher,³ G. Finley,³ A. Colonias,¹ and R.E. Wegner¹; ¹Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, ²Allegheny Health Network Department of Radiation Oncology, Pittsburgh, PA, ³Allegheny Health Network, Pittsburgh, PA

Purpose/Objective(s): Stereotactic ablative radiotherapy (SABR) is a noninvasive treatment strategy and the current standard of care for inoperable early stage non-small cell lung cancer (ES-NSCLC). NSCLC is a diverse group of malignancies with the predominant histologic subtypes of adenocarcinoma (ADC) and squamous cell carcinoma (SCC). Several retrospective analyses have demonstrated an association between SCC and increased rates of local failure following SABR. However, these previous investigations have shown incongruent results in regard to the histologic association of SCC with reduced overall survival. Therefore, we analyzed the national cancer database (NCDB) to compare overall survival in ES-NSCLC patients with ADC and SCC subtypes treated with SABR.

Materials/Methods: We queried the NCDB for ES-NSCLC (T1-2N0, Stage I-IIA) patients with pathologically confirmed SCC or ADC between the years 2004 – 2015 treated with 1-5 fractions of SABR to ablative doses (Biologically effective dose ≥ 100 Gy₁₀) in this IRB-exempt study. Univariable and multivariable analyses identified characteristics predictive of overall survival. Overall survival (OS) was calculated from the date of diagnosis to the date of last contact or death using Kaplan Meier curves to present the cumulative probability of survival, and log-rank statistics were used to assess statistical significance between groups. A propensity score analysis was used to account for any indication bias between the two histologic arms.

Results: Ultimately 15,310 ES-NSCLC patients with either ADC (n=9,009) or SCC (n=6,301) were eligible for analysis. Univariable analysis demonstrated a median overall survival of 44 months and 33 months ($p<0.0001$) and 5-year overall survival of 36% and 24% ($p<0.0001$) in patients diagnosed with ADC and SCC, respectively. Patients with ADC were less likely to have T2 lesions (OR: 0.70, 95% CI: 0.64-0.75, $p<0.0001$) and poorly differentiated grade (OR: 0.46, 95% CI: 0.42-0.51, $p<0.0001$). White race, male sex, T1 lesions, and age <75 years were also associated with improved survival. Patients with SCC still had worse survival on propensity score matched multivariable comparison ($p<0.0001$).

Conclusion: Our NCDB-based study is the largest known analysis examining the association between histology (SCC vs ADC) and survival outcomes in patients with ES-NSCLC treated with SABR. Both median and 5-year overall survival was inferior in patients with SCC, corroborating the results of previous studies. Randomized, prospective studies are needed to further validate these findings and potentially identify treatment strategies that may improve outcomes in this histologic subset.

Author Disclosure: S. Abel: None. S. Hasan: None. R. White: None. L. Schumacher: None. G. Finley: None. A. Colonias: None. R.E. Wegner: None.

	With Mutation		Without Mutation		P Value
	N (%)	Median PFS(Days)	N (%)	Median PFS(Days)	
NF1	6 (7.1%)	62	78 (92.8%)	180	0.0013
CD79a	8 (9.5%)	69	76 (90.4%)	169	0.0064
AKT3	10 (11.9%)	488	74 (88.1%)	129	0.0529

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Impact of Operability and Minimally Invasive Techniques on Post-Treatment Mortality with SBRT & Surgery in Early Stage NSCLC



W.A. Stokes,¹ M.W. McDonald,¹ K.A. Higgins,¹ and C.G. Rusthoven, Jr;²
¹Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, ²Department of Radiation Oncology, University of Colorado Denver, Aurora, CO

Purpose/Objective(s): Among patients with early stage non-small cell lung cancer (ES-NSCLC), operability is both a crucial determinant in treatment selection and a potential confounder in retrospective analyses comparing surgery with non-surgical approaches such as stereotactic body radiotherapy (SBRT). We analyzed post-treatment mortality among operable and inoperable ES-NSCLC patients undergoing SBRT and surgical resection via open and minimally invasive techniques.

Materials/Methods: We identified 4 groups of ES-NSCLC patients from the National Cancer Database: 1) SBRT patients who were coded as being offered surgery but refusing it and were therefore presumed to be operable (SBRT-Op); 2) SBRT patients lacking these codes and therefore presumed to be inoperable (SBRT-InOp); 3) patients coded as receiving minimally invasive surgery (Surg-MI); 4) patients undergoing surgery without those codes and thereby presumed to receive open surgery (Surg-Open). Mortality rates at 30, 60, and 90 days post-treatment were calculated for each group, and then rates were compared to those of the SBRT-Op group using both pairwise chi-square comparisons and Cox multivariate regression (MVA) adjusting for demographic and clinical covariates.

Results: We abstracted 640 SBRT-Op patients, 11,151 SBRT-InOp patients, 24,570 Surg-MI patients, and 67,722 Surg-Open patients. There were significant baseline differences between groups, with surgical patients tending to be younger, privately insured, and wealthier. Crude mortality rates were not significantly different between SBRT groups at 30 days, but the difference became significant at 60 and 90 days (**Table**). Similar results were found on Cox MVA at each time point (**Table**). Both pairwise comparisons of crude mortality rates and Cox MVA demonstrated reduced risk of mortality among SBRT-Op patients compared to those undergoing surgery (**Table**). In comparing surgical groups, mortality was significantly lower among Surg-MI patients compared to the Surg-Open cohort.

Conclusion: Operability status is strongly associated with outcomes among ES-NSCLC patients. Operable patients undergoing SBRT appear to experience minimal post-treatment mortality as compared to both their inoperable counterparts and to those patients undergoing surgery. Minimally invasive surgery is associated with lower post-treatment mortality compared to open procedures.

Author Disclosure: W.A. Stokes: None. M.W. McDonald: Emory Proton Therapy Center. K.A. Higgins: Consultant; Astra Zeneca. C.G. Rusthoven: None.

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Stereotactic Body Radiotherapy versus Local Tumor Ablation for Early-Stage Non-Small Cell Lung Cancer



B.J. Ager, S. Scheick, J.D. Gruhl, R. Tao, K.E. Kokeny, and Y.J. Hitchcock; University of Utah Huntsman Cancer Institute, Salt Lake City, UT

Purpose/Objective(s): Stereotactic body radiotherapy (SBRT) has emerged as a standard-of-care treatment modality for medically inoperable early-stage non-small cell lung cancer (NSCLC). Interventional radiological procedures achieving local tumor ablation (LTA) are frequently considered alternatives to SBRT, however comparative effectiveness data are lacking. We sought to compare overall survival within the National Cancer Database (NCDB) for those receiving SBRT versus LTA.

Materials/Methods: The NCDB was queried from 2004-2015 for adults with non-metastatic, node negative invasive adenocarcinoma or squamous cell carcinoma of the lung with primary tumor size ≤ 5 cm who did not undergo surgery and received SBRT or LTA. SBRT was defined as any of the following: 34 Gy in 1 fraction, 54 Gy in 3 fractions, 48 Gy in 3 fractions, 45 Gy in 3 fractions, 50 Gy in 4 fractions, 48 Gy in 4 fractions, 55 Gy in 5 fractions, or 50 Gy in 5 fractions. LTA included laser ablation, cryotherapy, electrocautery/fulguration, and local tumor ablation not otherwise specified. Patients receiving both SBRT and LTA were excluded. Clinical and demographic factors were compared with Pearson's chi-squared and multivariate logistic regression analyses. Propensity-score matching by age, sex, race, Charlson-Deyo Comorbidity Score, tumor size, histology, grade, and facility type was performed with inverse probability of treatment weighting. Overall survival was assessed using Kaplan-Meier analysis and Cox proportional hazards modeling.

Results: Of the 16,069 patients meeting criteria, 14,880 (93%) received SBRT and 1,189 (7%) received LTA. After propensity-score matching, SBRT was associated with improved OS relative to LTA on doubly-robust multivariate analysis (HR 0.75, $p < 0.001$). Female gender (HR 0.73, $p < 0.001$) and non-Caucasian race (HR 0.75, $p = 0.001$) were also associated with improved OS, whereas increasing age (HR 1.01, $p = 0.001$), Charlson-Deyo Comorbidity Score (Score = 2 HR 1.23, $p = 0.024$; Score ≥ 3 HR 1.98, $p < 0.001$), tumor size > 2 cm (2.1 – 3 cm HR 1.24, $p = 0.001$; 3.1 – 5 cm HR 1.55, $p < 0.001$), and tumor grade (moderately differentiated HR 1.42, $p = 0.001$; poorly differentiated/undifferentiated HR 1.48, $p < 0.001$) were associated with worse OS. On multivariate logistic regression analysis, patients receiving LTA were more likely to have a Charlson-Deyo Comorbidity Score of ≥ 1 (OR 1.33, $p = 0.001$), whereas those with tumors > 2 cm (2.1 – 3 cm OR 0.62, $p < 0.001$; 3.1 – 5 cm OR 0.36, $p < 0.001$) and those treated at an academic institution (OR 0.78, $p 0.010$) were more likely to receive SBRT.

Conclusion: SBRT was associated with improved OS when compared to local tumor ablation for patients with early-stage inoperable NSCLC within a matched cohort from the NCDB. These results are hypothesis-generating and warrant prospective validation.

	30-Day Mortality					60-Day Mortality					90-Day Mortality				
	Crude Rate		Cox MVA			Crude Rate		Cox MVA			Crude Rate		Cox MVA		
	%	p	HR	95%CI	p	%	p	HR	95%CI	p	%	p	HR	95%CI	p
SBRT-Op	0.2	-	1.00	-	-	0.3	-	1.00	-	-	0.8	-	1.00	-	-
SBRT-InOp	0.5	0.40	3.19	0.44-23.0	0.25	1.6	0.03	4.73	1.17-19.1	0.03	2.7	0.01	3.19	1.32-7.72	0.01
Surg-MI	1.3	0.01	11.3	1.59-80.8	0.02	1.9	<0.01	8.13	2.02-32.7	<0.01	2.3	0.01	3.91	1.62-9.45	<0.01
Surg-Open	2.0	<0.01	16.1	2.26-114	<0.01	2.9	<0.01	12.3	3.07-49.3	<0.01	3.4	<0.01	5.81	2.41-14.0	<0.01

Author Disclosure: B.J. Ager: None. S. Scheick: None. J.D. Gruhl: None. R. Tao: None. K.E. Kokeny: Consultant; Merit Medical. Speaker's Bureau; Merit Medical. Stock; Merit Medical, Bard. Y.J. Hitchcock: None.

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Outcomes after lung stereotactic body radiotherapy with and without pathologic confirmation



J.R. Wilkie,^{1,2} D. Owen,¹ R. Lipson,³ S. Jolly,¹ M.C. Johnson,⁴ and C.H. Chapman^{1,5}; ¹Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, ²Veterans Administration Ann Arbor Healthcare System, Ann Arbor, MI, ³Center for Clinical Management Research, Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, MI, ⁴Wayne State University School of Medicine, Detroit, MI, ⁵Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, MI

Purpose/Objective(s): Stereotactic body radiotherapy (SBRT) is increasingly being used in medically non-operable patients with early stage non-small cell lung cancer (NSCLC). Although pre-treatment pathologic confirmation (PC) is preferred, biopsies may be non-diagnostic or avoided altogether due to unfavorable tumor locations and medical comorbidities. Consequently, some patients are treated without pathologic confirmation. Since a proportion of these empirically treated patients may not actually have malignancy, it is important to understand how they ultimately fare clinically. In this study, we examined trends and outcomes in a large national sample of veterans with early stage NSCLC treated with SBRT with and without pathologic confirmation.

Materials/Methods: We identified 1,918 patients treated with lung SBRT for AJCC 7th edition cT1-T2aN0M0 NSCLC in the Veterans Affairs Central Cancer Registry from 2008-2015. We quantified the number of total cases and the percentage of cases treated without PC by year of diagnosis. We used logistic regression to assess for association between biopsy receipt, clinical, and demographic variables, and Cox proportional hazards modeling to compare overall survival between the PC and non-PC groups.

Results: The number of patients treated with SBRT for early stage NSCLC in this registry increased more than four-fold over the study period. Overall, 18% percent (n = 347) of patients were treated without PC, ranging from 12% in 2009 to 22% in 2015. Mean age was 71.5 v. 72.2 years in the PC and non-PC groups, respectively. Less than one percent of patients in the non-PC group were never smokers, compared to 2.5% in the PC group. Stage T1 patients were more likely to undergo treatment without PC (OR 2.97, $p < 0.001$) than stage T2 patients, with no significant age differences. Stage T2 (HR 1.23, $p = 0.01$) and increasing age (HR 1.02, $p < 0.001$), but not PC, were associated with an increased hazard of death.

Conclusion: Lung SBRT use for early stage NSCLC has greatly increased over the past decade within the Veterans Health Administration. The proportion of patients being treated without pathologic confirmation also appears to be increasing, to approximately 1 in 5 veterans. This is substantially higher than published rates from national non-VA populations, possibly due to increased comorbidities in this cohort of veterans. There was no difference in overall survival among patients with and without pathologic confirmation, which may suggest that some non-malignant lesions were treated in the non-PC group, compensating for the presumed increased comorbidities in this group. Future studies should examine optimizing clinical decision making, cost-effectiveness and toxicity rates in patients treated with lung SBRT without pathologic confirmation.

Author Disclosure: J.R. Wilkie: None. D. Owen: None. R. Lipson: None. S. Jolly: None. M.C. Johnson: None. C.H. Chapman: Research Grant; National Cancer Institute; National Medical Association.

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Early Outcomes of Patients with Locally-Advanced Non-small Cell Lung Cancer Treated with Intensity-Modulated Proton vs. Intensity-Modulated Radiation Therapies: A Single-Institution Experience



N.Y. Yu,¹ T.A. DeWees,¹ C. Liu,¹ R.S. Bhangoo,¹ T.B. Daniels,¹ J.B. Ashman,¹ H.J. Ross,² H.R. Paripati,³ J.X. Ding,¹ W. Liu,¹ S.E. Schild,¹ and T.T.W. Sio¹; ¹Department of Radiation Oncology, Mayo Clinic, Phoenix, AZ, ²Department of Hematology and Medical Oncology, Mayo Clinic, Phoenix, AZ, ³Department of Hematology and Medical Oncology, Phoenix, AZ

Purpose/Objective(s): Few studies have investigated the use of active-scanning proton beam therapy (PBT) in patients with locally advanced non-small cell lung cancer (NSCLC). We report the early clinical outcomes and toxicities of intensity-modulated proton therapy (IMPT) vs. intensity-modulated radiation therapy (IMRT) in patients with locally-advanced NSCLC.

Materials/Methods: Seventy-nine patients with locally-advanced NSCLC underwent definitive IMPT (42%) or IMRT (58%) from 2016-2018 at our institution. Patient characteristics were analyzed with chi-squared tests and comparative statistics. Kaplan-Meier survival curves were calculated for locoregional recurrence-free (LRFS), distant metastasis-free (DMFS), and overall (OS) survival rates since the date of first radiation therapy (RT). Acute and subacute toxicities were recorded by CTCAE v4.03.

Results: Median follow-up since date of first RT was 8.5 months. Eighty percent of patients had Stage III NSCLC. Median conventionally fractionated RT dose was 60 Gy (range, 52-66 Gy), and 65% of patients received concurrent chemotherapy (re-irradiation patients, 15%). At baseline, the IMPT cohort was older (75.8 vs. 69.2, $p=0.01$), more often had oxygen-dependent COPD (18% vs. 2%, $p=0.02$), and more often received re-irradiation as definitive treatment than their IMRT counterpart (27% vs. 9%, $p=0.04$). At 1 year, the IMPT and IMRT cohorts had similar LRFS (86% vs. 69%, $p=0.11$), DMFS (71% vs. 68%, $p=0.58$), and OS (68% vs. 65%, $p=0.87$). On multivariate analyses controlling for baseline toxicity, more severe COPD was positively associated with any grade 3 or higher toxicity at the end of RT (odds ratio 8.6; 95% confidence interval, 1.3-57.5; $p=0.02$), and older age was positively associated with any grade 3 or higher toxicity 3 months after RT (odds ratio 1.1; 95% CI, 1.0-1.3; $p<0.01$). There were no significant differences in grade 3 or 4 toxicities between IMPT and IMRT at 3 months after RT (5 vs. 4 patients, $p=0.47$, respectively). Regardless of RT modality, there were no treatment-related grade 5 toxicities.

Conclusion: Patients in the IMPT cohort were older, had increased rates of oxygen-dependent COPD, and more often received definitive treatment as re-irradiation when compared to the IMRT cohort. Despite these poor risk factors, our early experience suggests that IMPT and IMRT have comparable clinical outcomes and toxicity profiles in patients with locally-advanced NSCLC. Our findings suggest that active-scanning PBT is a safe and efficacious treatment option for primary or recurrent locally-advanced NSCLC and should be strongly considered for patients with older age and/or moderate to severe cardiopulmonary comorbidities.

Author Disclosure: N.Y. Yu: None. T.A. DeWees: None. C. Liu: Research Fellow; Mayo Clinic. R.S. Bhangoo: None. T.B. Daniels: None. J.B. Ashman: None. H.J. Ross: None. H.R. Paripati: None. J.X. Ding: None. W. Liu: Research Grant; NIH/NCI, The Lawrence W. and Marilyn W. Matteson Foundation, by The Kemper and Ethel Marley Foundation, Arizona Biomedical Research Commission. S.E. Schild: Research Grant; Alliance. Honoraria; uptodate. Travel Expenses; Alliance; NCCN

guideline panel on non-small cell lung cancer. Reviews NCI sponsored cooperative lung cancer trials; NCI thoracic malignancy steering committee. **T.T. Sio:** I provide strategic and scientific recommendations as a member of their Advisory Board; Novacure, Inc.

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Treatment Allocation Modeling and Risk-Stratified Outcomes for Clinical Stage I Non-small Cell Lung Cancer Patients Receiving Surgery versus Stereotactic Body Radiation Therapy



P. Samson,¹ C.G. Robinson,² W.R. Kennedy,² P. Gabani,² M.C. Roach, Jr,³ J.D. Bradley,³ B. Kozower,⁴ V. Puri,⁴ and B. Meyers⁴; ¹Washington University in St. Louis, Department of Radiation Oncology, St. Louis, MO, ²Washington University School of Medicine, Department of Radiation Oncology, St. Louis, MO, ³Washington University School of Medicine, St. Louis, MO, ⁴Washington University School of Medicine, Division of Cardiothoracic Surgery, St. Louis, MO

Purpose/Objective(s): Patients with stage I non-small cell lung cancer (NSCLC) are often categorized as operable, high-risk operable, or inoperable for consideration of treatment allocation to surgery or stereotactic body radiation therapy (SBRT). The aim of this study is to develop a model of treatment allocation based on physiologic characteristics, and to compare short and long-term outcomes among different risk-strata.

Materials/Methods: Stage I NSCLC patients treated at a single high-volume institution from 2007 to 2015 were retrospectively reviewed after IRB approval. Multivariable logistic regression was performed to identify physiologic factors independently associated with receipt of surgery or SBRT. From this regression model, propensity scores were assigned to each patient to describe their likelihood of allocation to SBRT, with 0 indicating low likelihood of receiving SBRT, and 1 indicating the highest likelihood of SBRT allocation. The propensity scores were divided into quintiles and patients' short- and long-term outcomes were compared based on their risk strata.

Results: From 2007-2015, 662/1132 (58.5%) clinical Stage I NSCLC patients received surgery, while 470/1132 (41.5%) received SBRT. SBRT patients were more likely to be older (median age, 74 years vs 67, $p<0.001$), have a diagnosis of congestive heart failure (CHF, 14.7% vs 1.7%, $p<0.001$), diabetes (23.0% vs 16.8%, $p=0.009$), and have a lower FEV1% predicted value (51% versus 82%, <0.001). On multivariable analysis, factors independently associated with receiving SBRT included increasing age (per year odds ratio, OR: 1.12) and CHF (OR 10.3), all $p<0.001$. Increasing FEV1% predicted was associated with a decreased likelihood of SBRT (per % increase OR: 0.93 $p<0.001$). From this model, propensity scores for treatment allocation were calculated for each patient, which were then divided into quintiles. Surgical patients with propensity scores in the fifth quintile were significantly more likely to receive sublobar resection than surgical patients with scores in the first quintile, 52% versus 15%, $p<0.001$. Additionally, surgical patients in the fifth quintile had a higher rate of post-operative pulmonary complications than first quintile patients (34.8% versus 8.5%, $p=0.03$). 3-year overall survival (OS) for surgical patients in the first quintile was 73%, while for the fifth quintile surgical patients was 38%, $p<0.001$.

Conclusion: Clinical stage I NSCLC surgical patients with a high propensity for SBRT allocation are more likely to have sublobar resection and experience higher rates of post-operative pulmonary complications. Additionally, surgical patients with a score indicating a high likelihood of SBRT allocation had decreased OS compared to those with a low likelihood of SBRT. Future directions include refining this model with prospective data to further categorize high-risk surgical patients.

Author Disclosure: P. Samson: Employee; Washington University; ImproveCareNow. C.G. Robinson: Research Grant; Varian Medical

Systems, Elekta. Speaker's Bureau; Varian Medical Systems, DFINE. Advisory Board; Radialogica. Travel Expenses; Varian Medical Systems, DFINE. Stock Options; Radialogica. **W.R. Kennedy:** None. **P. Gabani:** None. **M.C. Roach:** Travel Expenses; BTG, Varian, Elekta. **J.D. Bradley:** Research Grant; ViewRay, Inc, Mevion Medical Systems. Travel Expenses; Mevion Medical Systems. Organize NRG Oncology research agenda on lung cancer; American College of Radiology. **B. Kozower:** None. **V. Puri:** None. **B. Meyers:** None.

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Local therapy for oligoprogression in NSCLC patients being treated with osimertinib



C. Wang, H. Yu, V.W. Rusch, A. Rimner, and A.J. Wu; Memorial Sloan Kettering Cancer Center, New York, NY

Purpose/Objective(s): Osimertinib is a new standard treatment for metastatic NSCLC patients with sensitizing epidermal growth factor receptor (EGFR) mutations. Though progression-free survival is longer with osimertinib compared with earlier-generation tyrosine kinase inhibitors (TKIs) such as erlotinib, acquired resistance will ultimately occur. Data suggests that delivering local therapy to isolated sites of progression (oligoprogression) can prolong benefit from erlotinib, but outcomes with this strategy have not been reported for osimertinib.

Materials/Methods: We reviewed patients who received local therapy after progression on osimertinib (in first or second-line settings) and continued osimertinib treatment. Patients who never responded to osimertinib or did not receive local therapy for all progressing sites were excluded. Local therapy included stereotactic radiosurgery, conventional radiation therapy, or surgical resection. The endpoints of interest were time to subsequent progression, time to change in systemic therapy, and overall survival.

Results: We identified 25 patients who met the criteria (23 treated with radiation and 2 with surgery). Twenty-two (88%) of the patients had KPS ≥ 80 . Three (12%) patients were treated with osimertinib as first-line TKI therapy, and the other patients all had prior TKI treatment and developed EGFR-T790M mutations. Eighteen patients received local therapy for one site of progression, and the other 7 patients had 2 or 3 treatment sites. There were 34 oligoprogressive lesions treated in total, with 13 (38%) of them in lung and 12 (35%) of them in bone. The median follow-up time was 8.0 (95%CI 6.3-9.7) months. Fourteen of the 25 patients progressed after local therapy during the study period, and five of them died. For the whole cohort, the median time to progression after local therapy was 4.9 (95%CI 2.8-7.0) months, and the median time from local therapy to systemic therapy change was 7.8 (95% CI 4.4-11.1) months. Patients with only one oligoprogressive site had a trend of longer time to progression (8.4 vs 4.0 months, $p=0.06$) and longer time till systemic therapy change (12.0 vs 5.9 months, $p=0.07$), compared to patients with 2-3 oligoprogressive sites. The median overall survival after local therapy was 19.1 (11.2-27.1) months.

Conclusion: Local therapy can facilitate continued osimertinib therapy in patients with oligoprogression, particularly in patients with a single site of progression. Given that most patients in this study were receiving osimertinib after first-line TKI failure and would have limited options for further systemic treatment, this strategy warrants further study.

Author Disclosure: C. Wang: None. H. Yu: Research Grant; Lilly, AstraZeneca, daichi, Pfizer and Novartis. V.W. Rusch: Research Grant; Genelux; American College of Surgeons, IASLC. A. Rimner: Research Grant; Varian Medical Systems, Boehringer Ingelheim, Pfizer, AstraZeneca. Advisory Board; AstraZeneca, Merck. A.J. Wu: Research Grant; CivaTech Oncology, Inc. Consultant; AstraZeneca. Travel Expenses; AlphaTau Medical.

POSTER PRESENTATIONS

LBA1

Real-world Performance of Blood-Based Proteomic Profiling in Frontline Immunotherapy Treatment in Advanced stage NSCLC



P. Rich,¹ J. Roder,² J. Dubay,³ D. Oubre,⁴ E.K. Pauli,⁵ J.M. Orsini,⁶ E.S. Santos,⁷ M. Coleman,⁸ W. Khan,⁹ W. Akerley,¹⁰ R.D. Siegel,¹¹ L. Traylor,² and P. Walker¹²; ¹Cancer Treatment Centers of America, Newnan, GA, ²Biodesix, Boulder, CO, ³Lewis & Faye Manderson Cancer Center at DCH Regional Medical Center, Tuscaloosa, AL, ⁴Pontchartrain Cancer Center, Covington, LA, ⁵Clearview Cancer Institute, Huntsville, AL, ⁶Essex Oncology, Belleville, NJ, ⁷Lynn Cancer Institute, Boca Raton, FL, ⁸Clinical Research Associates, Lake Success, NY, ⁹Lake City Cancer Care, LLC, Lake City, FL, ¹⁰Huntsman Cancer Hospital, Salt Lake City, UT, ¹¹St. Francis Cancer Center, Greenville, SC, ¹²East Carolina University, Greenville, NC

Purpose/Objective(s): Immune checkpoint inhibitors (ICI) have improved outcomes for many advanced stage NSCLC patients. Patients with a PD-L1 score $\geq 50\%$ are candidates for either ICI monotherapy or in combination with chemotherapy, whereas only the combo is FDA approved for PD-L1 $< 50\%$. There is a need for improved biomarkers as other ICI combo therapies are approved. In a prospectively designed observational study (NCT03289780), the ability of a clinically validated blood-based proteomic test to predict outcomes for ICI therapy was assessed.

Materials/Methods: The study includes 33 US sites having enrolled 2100 patients to date in a registry style design allowing NSCLC patients with all stages and lines of therapy to enroll. Patient characteristics, therapeutic decisions, staging, disease monitoring metrics and available biomarker data have been collected and patients are being followed for 18 months. All enrolled patients receive blood-based proteomic testing (proteomic poor or proteomic good result) prior to therapy initiation. An interim analysis of secondary and exploratory endpoints was performed after 1 year follow up of the first 1000 enrolled patients following a pre-specified analysis plan. Overall survival (OS) was summarized by median and 95% confidence interval (CI) by Kaplan-Meier methods and compared between proteomic-defined subgroups by Cox Proportional hazard ratios and p values and reported in months (mo). Here we report the OS results from a subset of patients with advanced stage NSCLC (IIIB and higher) treated with frontline ICI regimens (n = 85; all frontline therapies n = 419).

Results: All ICI treated patients had a median OS (mOS) of 14.8 mo (CI: 7.8 - und); 53% male, 53% PD-L1 $\geq 50\%$, 45% ≥ 65 years, 76% ECOG PS 0 or 1. In patients with a proteomic good (PG) result (n = 54), mOS was not reached (CI: 14.8 - und) compared to 4.1 mo (CI: 2.0 - 7.8) for those with a proteomic poor (PP) result (n = 31); HR = 0.33 (CI: 0.18 - 0.61), p < 0.001. For ICI monotherapy (n = 46), mOS was 9.3 mo (CI: 4.1 - und) and for ICI with chemotherapy (n = 33), mOS was not reached (CI: 12.4 - und). In the ICI monotherapy subgroup, patients with a PG result (n = 28) experienced a mOS of 14.6 mo (CI: 8.0 - und) compared to 3.3 mo (CI: 1.4 - 7.0) for patients with a PP result (n = 18); HR = 0.45 (CI: 0.21 - 0.96), p = 0.039. In patients receiving ICI/chemotherapy combo, mOS was not reached (CI: 15.4 - und) for those with a PG result (n = 23) versus mOS of 5.9 mo (CI: 1.9 - und) in patients with a PP result (n = 10); HR = 0.23 (CI: 0.07 - 0.74), p = 0.014. The proteomic test was not significantly associated with PD-L1 status and was predictive of outcomes for ICI treatment when adjusted for PD-L1.

Conclusion: Blood-based proteomic testing may provide clinically meaningful information for immunotherapy treatment selection in NSCLC.

Author Disclosure: P. Rich: None. J. Roder: Employee; Biodesix. Stock Options; Biodesix. Patent/License Fees/Copyright; Biodesix. Officer; Biodesix. J. Dubay: None. D. Oubre: Owner; Pontchartrain Cancer Center. Board; Quality Cancer Care Alliance, Community Oncology Association, Coalition of Hematology/Oncology Practices. E.K. Pauli: None.

J.M. Orsini: Paid speaker; Astellas, Pfizer. Honoraria; Astellas, Pfizer. Director Oncology; New Jersey Urology. E.S. Santos: None. M. Coleman: Speaker's Bureau; Pharmacyclics, Gilead, Celgene, Bayer. Advisory board; Pharmacyclics, Celgene, Bayer. W. Khan: Partnership; Lake City Cancer Center. W. Akerley: None. R.D. Siegel: None. L. Traylor: Stock Options; Biodesix. ; Biodesix. P. Walker: Speaker's Bureau; Genentech.

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Analysis of Real-World PD-L1 Testing for Clinical Use in Patients with Lung Cancer



G.S. Krigsfeld,¹ K. Zerba,¹ V. Chizhevsky,² J.W. Ragheb,² and J. White¹; ¹Bristol-Myers Squibb, Princeton, NJ, ²NeoGenomics Laboratories, Inc., Aliso Viejo, CA

Purpose/Objective(s): Targeting the programmed death-1/programmed death ligand 1 (PD-1/PD-L1) pathway has improved clinical outcomes, expediting the US FDA approval of 5 agents as treatment for several tumor types. PD-L1 immunohistochemistry (IHC) diagnostic assays have been developed to guide treatment with anti-PD-1/PD-L1 agents. The Dako PD-L1 IHC 22C3 pharmDx and Ventana PD-L1 (SP142) assays are FDA-approved diagnostics for non-small cell lung cancer (NSCLC) as a companion to pembrolizumab and complementary to atezolizumab, respectively. The Dako PD-L1 IHC 28-8 pharmDx is approved for nonsquamous NSCLC, complementary to nivolumab. We sought to overcome barriers to PD-L1 testing by characterizing the use of 22C3, 28-8, and SP142 PD-L1 IHC assays on real-world lung cancer samples.

Materials/Methods: The analysis was performed between October 2015 and March 2018 based on a dataset of 55,652 tumor samples. Unique identifiers were used to associate clinical characteristics with PD-L1 expression results. A total of 24,210 PD-L1 IHC tests were performed on samples from 21,224 patients with lung cancer based on the manufacturer's protocols for NSCLC. Test success was defined as the presence of adequate tumor sample with quantifiable PD-L1 expression. Turnaround time (TAT) was defined as the time from receipt of the test specimen to test-report delivery to the requester.

Results: Between October 2015 and March 2018, the frequency of quarterly PD-L1 testing increased >4-fold, with an average TAT of 3.1 days for all tests. Quantifiable PD-L1 results were achieved for 96.9% of the 21,224 patients. Test success ranged between 93.1% and 96.8% for all three assays. The 22C3 assay was used in 21,528 (88.9%) of the total 24,210 PD-L1 tests performed, while the 28-8 and SP142 assays were used in 2405 (9.9%) and 277 (1.1%) of tests, respectively. Furthermore, 77.8% of patients tested had lung biopsies as opposed to biopsies from other sites (e.g., lymph nodes). The distribution and prevalence of tumor PD-L1 expression were observed across the dynamic range. Additional analyses on the prevalence of PD-L1 expression in this real-world setting will be presented.

Conclusion: PD-L1 testing rates in the US have increased over time. Most patients tested received a quantifiable PD-L1 result and, despite the increased demand over time, the majority of tests were returned to the requester in 2–4 days. Moreover, these real-world data demonstrate comparable success rates of PD-L1 testing by the 22C3, 28-8, and SP142 assays. These findings provide context on the evolution of PD-L1 testing and support the continued adoption of PD-L1 testing by IHC as a quality diagnostic for patients with lung cancer.

Author Disclosure: G.S. Krigsfeld: Stock Options; Bristol-Myers Squibb. K. Zerba: None. V. Chizhevsky: Independent Contractor; NeoGenomics Laboratories. Stock; Seattle Genetics. Stock Options; NeoGenomics Laboratories. J.W. Ragheb: None. J. White: Stock; Clovis, Tesaro.

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A Comparative Study of the PD-L1 IHC 22C3 and 28-8 Assays on Lung Cancer Samples



G.S. Krigsfeld,¹ K. Zerba,¹ J. Novotny, Jr,¹ V. Chizhevsky,² J.W. Ragheb,² and J. White¹; ¹Bristol-Myers Squibb, Princeton, NJ, ²NeoGenomics Laboratories, Inc., Aliso Viejo, CA

Purpose/Objective(s): Immune checkpoint inhibitors targeting the programmed death-1/programmed death ligand 1 (PD-1/PD-L1) pathway have improved clinical outcomes in patients with cancer. Testing for PD-L1 with immunohistochemistry (IHC) is performed to inform therapy decisions. Among the FDA-approved PD-L1 IHC diagnostic assays, the Dako PD-L1 IHC 22C3 pharmDx assay is approved as a companion diagnostic to pembrolizumab in non-small cell lung cancer (NSCLC) and the Dako PD-L1 IHC 28-8 pharmDx assay as a complementary diagnostic to nivolumab for nonsquamous NSCLC. Previous studies have compared the 2 assays in NSCLC and urothelial carcinoma. Here, we present a comparison of the 28-8 and 22C3 assays on the largest real-world dataset of lung cancer samples reported to date.

Materials/Methods: The analysis was performed between October 2015 and March 2018 based on a dataset of 55,652 tumor samples. Unique identifiers linked clinical characteristics with PD-L1 expression results. PD-L1 testing was performed on biopsy samples from 21,224 patients with lung cancer based on the manufacturer's protocols for NSCLC. Concordance evaluation was performed on the 1506 samples that had evaluable paired results from single tests with 28-8 and 22C3. Repeat tests on the same platform were excluded. Overall, positive, and negative percentage agreement (OPA, PPA, and NPA, respectively) were evaluated at the $\geq 1\%$ PD-L1 expression level for tumor cell membrane scoring. Higher expression thresholds are also being evaluated.

Results: High concordance at $\geq 1\%$ tumor PD-L1 expression was observed between the 28-8 and 22C3 assays across paired samples, with an observed OPA of 96.2% for comparisons (Table 1). Passing–Bablok regression analysis showed that PD-L1 expression data were highly correlated between the 2 assays (Spearman's $r = 0.96$). Further analyses on concordance by biopsy site between the 2 assays will be presented.

Conclusion: These real-world data demonstrate the high level of concordance between the PD-L1 IHC 28-8 and 22C3 pharmDx assays on lung cancer samples. These findings support the potential interchangeability of these assays for assessing tumor cell membrane PD-L1 expression in patients with lung cancer, providing confidence for healthcare providers in assessing patient treatment options.

Table 1

$\geq 1\%$ tumor PD-L1		Dako 28-8 pharmDx		
		Positive	Negative	Total
Dako 22C3 pharmDx	Positive	880	28	908
	Negative	30	568	598
	Total	910	596	1506
Using 28-8 as the reference		Using 22C3 as the reference		
	n/N	% (95% CI)	n/N	% (95% CI)
PPA	880/910	96.7 (95.3–97.7)	880/908	96.9 (95.6–97.9)
NPA	568/596	95.3 (93.3–96.7)	568/598	95.0 (92.9–96.5)
OPA	1448/1506	96.2 (95.1–97.0)	1448/1506	96.2 (95.1–97.0)

Author Disclosure: G.S. Krigsfeld: Stock Options; Bristol-Myers Squibb. K. Zerba: None. J. Novotny Jr: None. V. Chizhevsky: Independent Contractor; NeoGenomics Laboratories, Inc. Stock; Seattle Genetics. Stock Options; NeoGenomics Laboratories, Inc. J.W. Ragheb: None. J. White: Stock; Clovis, Tesaro.

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Immunomodulatory Effect of Tumor Treating Fields (TTFields) Results in Enhanced Antitumor Efficacy When Combined with Anti-PD-1 Therapy in Mouse Model of Lung Cancer



T. Voloshin,¹ S. Davidi,¹ Y. Porat,¹ A. Shteingauz,¹ M. Munster,¹ N. Kaynan,¹ R.S. Schneiderman,¹ C. Tempel Brami,¹ E. Zeevi,¹ K. Gotlib,¹ S. Cahal,¹ A. Itzhaki,¹ M. Giladi,² E. Kirson,² U. Weinberg,¹ A. Kinzel,³ and Y. Palti¹; ¹Novocure, Haifa, Israel, ²Novocure Ltd, Haifa, Israel, ³Novocure, Munich, Germany

Purpose/Objective(s): Tumor Treating Fields (TTFields) are a clinically applied anti-neoplastic treatment modality delivered via noninvasive application of low intensity, intermediate frequency, alternating electric fields. This therapy is approved for the treatment of patients with glioblastoma and pilot studies have demonstrated the safety as well as preliminary effectiveness of TTFields application in patients with non-small cell lung cancer and mesothelioma. Here we evaluated the potential of TTFields therapy to induce immunogenic cell death (ICD) and evaluate the efficacy of concurrent application of TTFields and anti-PD-1 therapy in murine Lewis lung carcinoma (LLC-1) orthotopic model.

Materials/Methods: Cultured murine cells were treated with TTFields using the invitro system. ICD was characterized by the exposure of calreticulin (CRT) on the cell surface, secretion of adenosine triphosphate (ATP), and release of the chromatin-binding protein high mobility group B1 (HMGB1). For detection of ER stress, phosphorylation of the translation initiation factor eIF2 α was assessed. Dendritic cells (DCs) were co-incubated with TTFields treated LLC-1 cells and phagocytosis by DCs and DCs maturation were evaluated. Mice orthotopically implanted with LLC-1 cells were treated with TTFields, the immune checkpoint inhibitor anti-PD-1 or a combination of the two modalities. Tumor volume was monitored and flow cytometry analysis was performed.

Results: Cancer cells that die under TTFields application exhibit release of HMGB1, ATP depletion from cells, and ER stress leading to CRT translocation to the cell surface. Moreover, we demonstrate that TTFields treated cells promote phagocytosis by DCs, DC maturation in vitro, and initiate inflammation in vivo. We also show that the combined treatment of lung tumor-bearing mice with TTFields plus the immune checkpoint inhibitor anti-PD-1 led to a significant decrease in tumor volume compared to anti-PD-1 alone or to the control group. A significant increase in CD45+ tumor infiltrating cells was observed in the TTFields plus anti-PD-1 group. These infiltrating cells, specifically macrophages and DCs, demonstrated upregulation of surface PD-L1 expression. Correspondingly, cytotoxic T-cells isolated from these tumors have shown higher levels of IFN- γ production relative to untreated mice.

Conclusion: Our results demonstrate the potential of TTFields therapy to induce ICD. We also demonstrate robust efficacy of concurrent application of TTFields and anti PD-1 therapy in a mouse model of lung cancer. These data suggest that combining TTFields with anti-PD-1 might achieve tumor control by further enhancing antitumor immunity.

Author Disclosure: T. Voloshin: Stock Options; Novocure. S. Davidi: Stock Options; Novocure. Y. Porat: Stock Options; Novocure. A. Shteingauz: Stock Options; Novocure. M. Munster: Stock Options; Novocure. N. Kaynan: Stock Options; Novocure. R.S. Schneiderman: Stock Options; Novocure. C. Tempel Brami: Stock Options; Novocure. E. Zeevi: Stock Options; Novocure. K. Gotlib: Stock Options; Novocure. S. Cahal: Stock Options; Novocure. A. Itzhaki: Stock Options; Novocure. M. Giladi: Stock Options; Novocure. E. Kirson: Stock; Novocure. Stock Options; Novocure. CSO; Novocure. U. Weinberg: Stock Options; Novocure. VP R&D; Novocure. A. Kinzel: Stock Options; Novocure. VP Medical EMEA; Novocure. Y. Palti: Founder; Novocure. Stock; Novocure. Stock Options; Novocure. founder; Novocure.

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Heterogeneity of PD-L1 expression between invasive and lepidic components of lung adenocarcinomas



N. Majithia,¹ M.C. Aubry,¹ S. Murphy,¹ and A.S. Mansfield;¹ Mayo Clinic, Rochester, MN

Purpose/Objective(s): Immunotherapy has transformed the treatment of advanced stages of lung cancer and is being investigated pre-operatively in clinical trials. Programmed death ligand 1 (PD-L1) expression is utilized to predict response to immunotherapy, but questions remain regarding its reliability as a biomarker. Given the incorporation of immune checkpoint inhibitors into the management of earlier stages of disease, and the potential for PD-L1 expression to be involved with the invasive process, we sought to evaluate patterns of PD-L1 expression between lepidic and invasive components of resected adenocarcinomas (ADs).

Materials/Methods: A cohort of patients with resected primary ADs with lepidic and invasive patterns of growth were identified at our institution. PD-L1 expression of both immune and tumor cells within the lepidic and invasive regions of each sample were determined by IHC using the PD-L1 specific SP263 antibody. PD-L1 cutoffs of $\geq 1\%$ and $\geq 5\%$ were used to indicate positivity in separate analyses. Agreement statistics were utilized for analysis.

Results: Eighty-six ADs were included in the study. Positively staining immune and tumor cells were observed in 50 (58.1%) and 18 (20.9%) samples, respectively, using $\geq 1\%$ PD-L1 expression cutoff. This dropped to 9 (10.5%) and 12 (14.0%), respectively, with $\geq 5\%$ PD-L1 expression. PD-L1 positive immune cells were observed in 31 lepidic and 32 invasive patterns at $\geq 1\%$ cutoff, with an agreement of PD-L1 expression in 49 and disagreement in 37 samples ($\kappa = 0.073$). At $\geq 5\%$ cutoff this dropped to 3 lepidic and 7 invasive patterns; agreement in 78 and disagreement in 8 ($\kappa = 0.159$). PD-L1 positive tumor cells were observed in 11 lepidic and 15 invasive patterns at $\geq 1\%$ cutoff; agreement in 76 and disagreement in 10 ($\kappa = 0.549$). At the $\geq 5\%$ cutoff this dropped to 3 lepidic and 12 invasive patterns; agreement in 77 and disagreement in 9 ($\kappa = 0.365$).

Conclusion: Although levels of PD-L1 positivity were low in this cohort, there was generally poor agreement in PD-L1 expression between lepidic and invasive regions. The strongest agreement was observed between lepidic and invasive tumor cells, using PD-L1 $\geq 1\%$ as the cutoff. Tumor cells in invasive patterns tended to be more strongly PD-L1 positive compared to those in lepidic patterns, which may indicate that PD-L1 is upregulated during the invasive process for a subset of ADs.

Author Disclosure: N. Majithia: None. M. Aubry: None. S. Murphy: None. A.S. Mansfield: Advisory Board; Genentech, In, BMS, AbbVie. Member of committee; ASCO.

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Pooled analysis of 121 patients from two phase II trials in NSCLC and mesothelioma show the safety of Tumor Treating Fields applied to the thorax



G. Ceresoli¹ and M. Pless²; ¹*Istituto Clinico Humanitas IRCCS Rozzano (MI), Italy;* ²*Chefarzt Medizinische Onkologie, Winterthur, Switzerland*

Purpose/Objective(s): Tumor Treating Fields (TTFields), a non-invasive, loco-regional, antimetabolic treatment modality, is approved for glioblastoma. TTFields are delivered through transducer arrays applied non-invasively to the tumor region. In a phase 3 trial in newly diagnosed glioblastoma (GBM), TTFields added to temozolomide was not associated with any significant increase in systemic adverse events (AEs) versus temozolomide alone. The only treatment-related AE seen in TTFields-treated patients was localized dermatitis underneath the arrays. Mild-moderate dermatitis was reported in 52% of patients (2% had grade 3 skin toxicity). The safety of TTFields was analyzed in two phase I-II studies in non-small-cell lung cancer (NSCLC) [NCT00749346] and mesothelioma [NCT02397928].

Materials/Methods: TTFields studies included in this pooled analysis were EF-15 (n=41, advanced NSCLC; plus pemetrexed) and STELLAR (n=80, malignant pleural mesothelioma; plus platinum and pemetrexed). TTFields were applied 12 - 18 hours/day at a frequency of 150 kHz. All patients received standard of care systemic chemotherapy for their disease in addition to TTFields. Severity and frequency of AEs, and association with TTFields treatment were evaluated (CTCAE criteria version 4.0).

Results: Age of patients ranged from 27-78 years: STELLAR: 67 (27-78) and EF-15: 63 (44-78). Patients had an ECOG score of 0-1; 7 patients in the EF-15 study had ECOG 2. The incidence of grade 1-2 gastrointestinal (GI) toxicities was 27%. The most common low-grade GI toxicities were: Nausea (18%), vomiting (12%), constipation (12%) and diarrhea (6%). Grade 1-2 general disorders such as asthenia, fatigue and asthenia were common and occurred in 27% of all patients. Grade 3-4 dyspnea was reported in 6% of patients. These AEs were related to standard chemotherapy or underlying disease. Grade 1-2 cardiovascular AEs were 5%; arrhythmias were $\leq 1\%$ and there was only one case of severe arrhythmia (atrial flutter) reported, unrelated to TTFields. The only common TTFields-related adverse event was dermatitis beneath the transducer arrays. 25% patients had dermatological

AEs: Grade 1-2 dermatitis in 17% of and grade 3 dermatitis in 5% of patients. 2% of patients complained of grade 1-2 pruritus.

Conclusion: Treatment of solid tumors with TTFields at 150 kHz to the thorax did not result in serious AEs or treatment related pulmonary, cardiac, hematological or gastrointestinal toxicities. Expected dermatological toxicity beneath the device transducer arrays was seen in 25% patients and resolved after a short treatment break or termination of treatment. These safety results combined with encouraging survival outcomes support the potential use of TTFields as a treatment in NSCLC and mesothelioma.

Author Disclosure: G. Ceresoli: Travel Expenses; Novocure. M. Pless: None.

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Treatment of tracheobronchial amyloidosis with external beam radiation therapy



N.A. McDonnell,¹ R.K. Funk,¹ R.L. Foote,¹ S. Kalra,² and M.A. Neben-Wittich¹; ¹*Department of Radiation Oncology, Mayo Clinic, Rochester, MN;* ²*Department of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN*

Purpose/Objective(s): Isolated tracheobronchial amyloidosis (TBA) is a rare condition characterized by deposition of insoluble fibrillary proteins within the pulmonary tree. We previously reported a case series of seven patients treated with external beam radiation therapy (EBRT) with a favorable response to radiation.¹ Here we report treatment response for 10 additional patients and long-term follow-up for the initial seven patients, including our experience with re-irradiation in four patients.

Materials/Methods: After IRB approval, all patients treated with EBRT for tracheobronchial amyloidosis at our institution were identified. Data regarding symptoms, diagnosis, treatments, and side effects were collected from the electronic medical record.

Results: All 17 patients received 20 Gy in ten fractions to the involved tracheobronchial tree as their initial EBRT. Median follow up for the whole cohort was 48 months (range 5-223 months), and for the original seven patients was 92 mo (range 64-223 months). All patients had improvement or stabilization of symptoms post initial EBRT. Median time to symptomatic response was 3 months (range 0-9 months). Median duration of response after first treatment was 21 months (range 3-185). Responses were objectively measured by repeat pulmonary function tests, CT and bronchoscopy. Subjective and objective responses did not always correlate. Patients were considered for re-treatment if they had a relapse of symptoms, with or without worsening of airway amyloid deposition on CT or bronchoscopy. Retreatment was a further 20 Gy in ten fractions. Three patients received a second course of EBRT 4, 9, and 17 months after their initial treatment. For one patient, the second course of EBRT improved respiratory symptoms for 60 months. The other two patients had improved or stable symptoms for two and seven months but were then lost to follow-up. One patient received a second and third course of EBRT, at 76 and 117 months post initial EBRT, and had a good symptomatic response to each treatment. Grade 1 (n=9) or grade 2 (n=1) esophagitis was the most common acute side effect. Four patients had steroid-responsive cough and wheeze. Four patients experienced grade 1 fatigue. Toxicities from the second and third courses of EBRT were similar to the first. One patient developed a non-small cell lung cancer five years after treatment in the setting of a smoking history.

Conclusion: EBRT for TBA is well-tolerated, and the majority of patients experience symptomatic improvement. Re-irradiation is well tolerated and can be considered in carefully selected patients.

References

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Author Disclosure: N.A. McDonnell: None. R.K. Funk: None. R.L. Foote: Employee; Mayo Clinic. Consultant; Up to Date. Responsible for clinical practice, research and education; Mayo Clinic. Responsible for the written board examination questions for head, neck and skin cancer.; ABR. S. Kalra: Employee; Mayo Clinic. Editorial Board Member; Journal of Cardiopulmonary Rehabilitation and Prevention. M.A. Neben-Wittich: Employee; Mayo Clinic.

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The Combined Treatment of 150 kHz Tumor Treating Fields (TTFields) and Cisplatin or Pemetrexed Inhibit Mesothelioma Cells In Vitro

M. Munster,¹ R.S. Schneiderman,¹ Y. Porat,¹ T. Voloshin,¹ S. Davidi,¹ A. Shteingauz,¹ N. Kaynan,¹ E. Zeevi,¹ K. Gotlib,¹ M. Giladi,² E. Kirson,² U. Weinberg,¹ A. Kinzel,³ and Y. Palti¹; ¹Novocure, Haifa, Israel, ²Novocure Ltd, Haifa, Israel, ³Novocure, Munich, Germany

Purpose/Objective(s): Malignant pleural mesothelioma (MPM) is a rare thoracic solid tumor cancer that has been strongly linked to asbestos exposure. It has a long latency period of at least 20-30 years following exposure, and global incidence is still increasing in countries where asbestos is still in use. Surgical resection for patients with early stage MPM is considered standard therapy and radiation therapy offers only palliative benefit. For patients with advanced disease, combination chemotherapy with Cisplatin and Pemetrexed results in improvement in survival and quality of life, thus constituting the “standard of care”. Tumor Treating Fields (TTFields) therapy is an effective anti-neoplastic treatment modality delivered via noninvasive application of low intensity, intermediate frequency, alternating electric fields. TTFields are employed as a local treatment with the intent to target dividing cells by disrupting microtubules leading to mitotic catastrophe, abnormal chromosome segregation and the induction of different forms of cancer cell death. The aim of this work is to explore the potential of the use of TTFields alone and in combination with cisplatin or pemetrexed as a treatment for Mesothelioma.

Materials/Methods: MSTO-211H and NCI-H2052 cells were treated with various TTFields frequencies for 72 hours using the inovitro system. Efficacy of the combined treatment of TTFields and Cisplatin or Pemetrexed was tested by applying TTFields at the optimal frequency together with various drug concentrations. Cell counts, induction of apoptosis, and clonogenic potential were determined at the end of treatment.

Results: The optimal TTFields frequency leading to the highest reduction in cell counts was found to be 150 kHz for both MSTO-211H and NCI-H2052 cells. TTFields application (1.1 V/cm, 72 hours) at 150 kHz led to 51-65% reduction in cell counts and 40-55% reduction in the clonogenic potential in both NCI-H2052 and MSTO-211H cells. The combined treatment of TTFields and Cisplatin or Pemetrexed led to a significant reduction in cell count, induction of apoptosis and reduced clonogenic potential as compared to each modality alone (2-way ANOVA, P<0.05). Safety studies did not reveal any adverse event associated with 150 kHz TTFields application to the rat torso.

Conclusion: The results presented in this work demonstrate that TTFields can be an effective treatment against Mesothelioma cells and that the combination with cisplatin or pemetrexed may further enhance treatment efficacy. In accordance with these results, it was recently reported that patients treated by the combined treatment of TTFields with pemetrexed and cisplatin experienced improved overall survival as compared to historical control with no increase in systemic toxicity.

Author Disclosure: M. Munster: Stock Options; Novocure. R.S. Schneiderman: Stock Options; Novocure. Y. Porat: Stock Options; Novocure. T. Voloshin: Stock Options; Novocure. S. Davidi: Stock Options; Novocure. A. Shteingauz: Stock Options; Novocure. N. Kaynan: Stock Options; Novocure. E. Zeevi: Stock Options; Novocure. K. Gotlib: Stock Options; Novocure. M. Giladi: Stock Options; Novocure. E. Kirson: Stock; Novocure. Stock Options; Novocure. CSO; Novocure. U. Weinberg: Stock Options; Novocure. VP R&D; Novocure. A. Kinzel: Stock Options; Novocure. VP Medical EMEA; Novocure. Y. Palti: founder; Novocure. Stock; Novocure. Stock Options; Novocure. Founder; Novocure.

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Role of mTOR Inhibitor Everolimus in the Treatment of Metastatic Thymic Epithelial Tumors

J. Hellyer, S. Padda, and H.A. Wakelee; *Stanford Cancer Institute/Stanford University School of Medicine, Stanford, CA*

Purpose/Objective(s): Metastatic thymic epithelial tumors (TETs) are a rare, heterogenous group of tumors that present a treatment challenge.

Optimal treatment for metastatic disease after progression on platinum-based chemotherapy has yet to be determined. Efforts are underway to elucidate predictive biomarkers in TETs to help guide treatment options. There is emerging evidence to support the use of mTOR inhibitors in advanced TETs. We sought to describe a single-center experience with mTOR inhibitor everolimus in TETs.

Materials/Methods: All patients who were prescribed everolimus at our institution were abstracted from the electronic medical record. Patients were included if they were being treated for metastatic thymoma or thymic carcinoma. Charts were reviewed retrospectively and demographic data, duration of therapy, adverse events, prior treatment history and presence of autoimmune events were abstracted.

Results: Ten patients with TETs, including eight thymomas and two thymic carcinomas treated with everolimus were identified. All patients had been heavily pre-treated with an average of three lines of therapy prior to starting everolimus. Best response was stable disease in six patients. Three patients discontinued treatment due to adverse events (grade 3 mucositis and pancytopenia; intolerable grade 2 fatigue). The average length of treatment was 13 months (range 2 – 32 months). Most common side effects were mucositis and pancytopenia. Of the five patients with thymoma-related autoimmune conditions, three saw significant improvement (polyarthritis, pure red cell aplasia and enteropathy) while two others saw no change (myasthenia gravis and Good syndrome).

Conclusion: Patients with metastatic TETs who have progressed on standard chemotherapy appear to benefit from everolimus. Genetic testing of these tumors using targeted next generation sequencing panel STAMP is underway to define biomarkers that may predict response to mTOR inhibitors.

Author Disclosure: J. Hellyer: None. S. Padda: Research Grant; Forty Seven Inc, EpicentRx, Bayer. Advisory Board; AstraZeneca, Abbvie, G1 Therapeutics, Janssen. H.A. Wakelee: Research Grant; BMS, MedImmune/AstraZeneca. Consultant; AstraZeneca. Research support and consultant (uncompensated); Merck, Genentech; International Thymic Malignancies Interest Group.

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Treatment of thymic carcinoma with erlotinib and remarkable disease stabilization for 9 years: A case report

L. Taniwaki and S.D. Simon; *Hospital Israelita Albert Einstein, São Paulo, Brazil*

Purpose/Objective(s): Epidermal growth factor receptor (EGFR) is a transmembrane glycoprotein with intrinsic tyrosine kinase activity that mediates effects through several pathways and results in cell proliferation and differentiation. EGFR is overexpressed in many neoplasias and in some of these, studies have shown that associated EGFR mutations are predictive of clinical response to EGFR-tyrosine kinase inhibitors (TKIs). While advanced non-small cell lung cancer patients harboring EGFR mutations have a rapid and marked response to EGFR-TKIs, for thymic cancer this has not yet been well established.

Materials/Methods: We herein present a case of thymic cancer with EGFR mutation treated with erlotinib after failure with concurrent chemoradiation therapy.

Results: An asymptomatic and otherwise healthy 61yearold man, former smoker, was referred to our service because of a chest radiography with mediastinal enlargement. Computed tomography (CT) scan showed an anterior 6.7 x 6.5 x 4.2cm mediastinal mass and mediastinal lymph nodes measuring up to 1.1cm. Needle biopsy suggested a poorly differentiated carcinoma. Immunohistochemistry (IHC) was positive for AE1/AE3 and CK8; and negative for CK7, CK20, TTF1, chromogranin A, synaptophysin, CD45 and CD56. Bronchoscopy was normal and PET-CT showed only FDG uptake in the mediastinal mass.

The patient received concurrent chemoradiation therapy based on cisplatin plus etoposide with modest shrinkage of the tumor. Testing for EGFR mutation by polymerase chain reaction (PCR) and direct sequencing showed exon 19 deletion (deIE746-750). Subsequent chest CT showed stable disease but enlarged mediastinal lymph nodes up to 2.1cm.

The patient was begun on erlotinib 150mg daily with disappearance of the mediastinal lymphadenopathy and progressive shrinking and calcification of the mediastinal mass until 4.0cm. He has been receiving the drug continuously for 108 months with good tolerance, stable disease and no evidence of local recurrence or distal metastasis.

Recent pathology review with complementary IHC (p63+, CD5+, patchy CD117+, CD57- and TDT-) confirmed a squamous cell carcinoma of probable thymic origin.

Conclusion: Since the 90s, EGFR has been seen as a potential target for therapy because of the observation of EGFR overexpression by IHC in thymic epithelial tumors. However, no study found both EGFR mutations and good responses of TC to EGFR-TKIs.

Our patient has had an unusually prolonged response to erlotinib in second line treatment. It is the longest reported survival of an advanced TC patient with EGFR mutation. This case seems to be a bona-fide case of TC, due to absence of any lung lesion and IHC findings.

The current case encourages screening for EGFR mutations in TC and future studies to confirm the potential activity of targeted therapy for this malignancy.

Author Disclosure: L. Taniwaki: None. S.D. Simon: Coordinate the Entity in order to promote ethical practice of Oncology, policies to develop the Brazilian Oncology and continuing education to encourage the research in Brazil.; SBOC - Brazilian Society of Clinical Oncology.

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Breathing-motion-compensated stereotactic body radiation therapy for moving targets: Patterns of failure analysis



F. Wang,^{1,2} Y.S. Butler-Xu,³ W. Yap,⁴ S.S. Sood,³ M.J. Tennapel,⁵ H. Jiang,³ and R.K. Badkul⁵; ¹University of Kansas Medical Center, Kansas City, KS, ²The University of Kansas Hospital, Kansas City, KS, ³Department of Radiation Oncology, University of Kansas School of Medicine, Kansas City, KS, ⁴University of Kansas, Kansas City, KS, ⁵University of Kansas Medical Center, Kansas City, KS

Purpose/Objective(s): The influence of tumor motion on dose delivery in stereotactic body radiation therapy (SBRT) for lung cancer using 3-D arc therapy, fixed field intensity modulated radiation therapy, and volumetric modulated arc therapy has been studied, but its clinical impact has not been well defined. We retrospectively evaluated the patterns of failure for breathing-motion-compensated stereotactic body radiation therapy (SBRT) in the treatment of lung cancers.

Materials/Methods: Between May 2009 and July 2016, a total of 106 patients with early stage non-small cell carcinoma of the lung (NSCLC) were treated with breathing-motion-compensated SBRT. Patients were simulated with free-breathing 4-dimensional computed tomography (4-DCT) to generate internal target volume (ITV) for breathing motion compensation. The median ITV was 7.6 cc (0.55 – 206 cc), respectively. Median biologically effective dose (BED; $\alpha/\beta = 10$ Gy) prescribed to the planning target volume was 100 Gy (100 – 151 Gy). We analyzed local control, regional control, nodal control, freedom from metastasis, overall survival, and lung cancer specific survival based on target motion volume (calculated by subtracting GTV from ITV) as well as dosimetric parameters (BED, GTV, and ITV) and patient characteristics (age, history of other malignancies, tumor histology, T stage, lobe location, and PET scan parameters).

Results: Median follow up was 22 months (1- 95 months). The two-year rates of local control, regional control, nodal control, and freedom from metastasis were 93%, 94%, 77%, and 81%, respectively. Overall survival and lung cancer specific survival at 2 years were 81% and 96%, respectively. Median target motion volume was 0.8cc (0 – 16cc). Target motion volume was larger for tumors in the lower lobes ($p=0.01$) as well as tumors with larger GTV ($p<0.0001$). On univariate analysis, we found that higher target motion volume was a significant predictor for decreased local control ($p=0.0013$), nodal control ($p=0.0089$), freedom of metastasis ($p=0.0003$), and overall survival ($p=0.0091$). There was no correlation between target motion volume and incidence of pneumonitis ($p=0.4$) or rib fracture ($p=0.5$). Other factors examined were not predictors for

clinical outcome except for T stage (T1a predicted for higher local control ($p=0.0078$)) and PET volume (higher tumor volume on PET was associated with decreased nodal control ($p=0.0075$) and lung cancer specific survival ($p=0.027$)).

Conclusion: Our study demonstrates that target motion volume is a significant predictor for clinical outcome in patients with early stage NSCLC treated with breathing-motion-compensated SBRT. To our knowledge this is the first study to exhibit the potential clinical impact of target motion in NSCLC patients treated with SBRT. Further studies from the perspectives of physics and radiation biology are warranted.

Author Disclosure: F. Wang: None. Y.S. Butler-Xu: None. W. Yap: None. S.S. Sood: None. M.J. Tennapel: None. H. Jiang: None. R.K. Badkul: None.

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Assessing the Relationship of Background Lung Density on Outcome and Toxicity after Stereotactic Body Radiation Therapy



M.E. May, Jr,¹ S. Bhadury,² J. Gaskins,² and N.E. Dunlap¹; ¹University of Louisville School of Medicine, Department of Radiation Oncology, Louisville, KY, ²University of Louisville School of Public Health, Department of Bioinformatics & Biostatistics, Louisville, KY

Purpose/Objective(s): Stereotactic Body Radiation Therapy (SBRT) has become the standard of care in the use of radiation therapy (RT) for the treatment of early stage non-small cell lung cancer (NSCLC) in non-surgical candidates. Underlying lung disease from smoking is a major driving factor in the decision to treat these patients with definitive RT, however, there are questions as to how the hypoxic nature of emphysematous lung may impact control and toxicity with ablative dose radiation. We analyzed a cohort of patients who underwent definitive SBRT to determine what role underlying lung dysfunction plays in local control and treatment toxicity.

Materials/Methods: A retrospective analysis was performed on 83 patients treated with volumetric modulated arc therapy SBRT at our academic institution with at least 6 months of follow up. Low density lung tissue was used as a measure of emphysematous change and quantified by Hounsfield unit (HU) measurements of proximal (within 2 centimeters of tumor) and ipsilateral lung tissue. Baseline pulmonary function tests (PFTs) were used to further characterize baseline lung dysfunction, with clinically reported radiation pneumonitis (RP) and radiographic radiation fibrosis (RF) used to score toxicity. Patient demographics, smoking history, tumor location, baseline lung dysfunction, and clinical and radiographic manifestations of toxicity were analyzed with proportional odds regression models to assess predictors of toxicity. Cox regression models were used to assess progression free survival (PFS) in the form of in-field, lobar, mediastinal, and distant failures, as well as overall survival (OS).

Results: The median OS was 37.8 months, with 1- and 5-year OS of 83.4% and 33.3% respectively. Low density proximal and ipsilateral lung tissue directly correlate with pack year smoking history (Kendall correlation $p=0.005$, 0.013, respectively). PFTs did not significantly predict toxicity or outcome. Density did not affect for RP, but a reduction in RF with decreasing HU approached significance ($p=0.060$). No measure of lung dysfunction significantly affected OS or PFS for all comers, but did demonstrate a significant improvement of in-field control for both proximal (standardized HR: 0.324, 95% CI: 0.126-0.832, $p=0.019$) and ipsilateral (standardized HR: 0.375, CI: 0.176-0.799, $p=0.011$) low density lung tissue.

Conclusion: Emphysematous lung tissue in the area immediately proximal to a tumor and in the ipsilateral lung promotes increased local control in patients treated with SBRT for early stage NSCLC, with a protective effect against RF approaching significance. This may suggest that increased biologic dose eliminates the detrimental effect of hypoxia seen in conventional RT. Applying this analysis to a larger cohort is warranted to further elucidate the prognostic value of underlying lung dysfunction.

Author Disclosure: M.E. May: None. S. Bhadury: None. J. Gaskins: None. N.E. Dunlap: Honoraria; Osler Institute.

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Outcomes and Toxicities in a Military Community Setting Post Stereotactic Body Radiation Therapy (SBRT) for Early Stage Non-Small Cell Lung Cancer (NSCLC)



M. Chamberlin, A.R. Horn, and A. Reed; *Walter Reed National Military Medical Center, Bethesda, MD*

Purpose/Objective(s): We compared our institutional outcomes for early stage non-small cell lung cancer treated with definitive SBRT to recently published prospective data in order to determine the generalizability to our military community setting. The United States military represents a unique patient population to study lung cancer outcomes due to universal access to care and routine follow-up.

Materials/Methods: We retrospectively reviewed all patients who received definitive lung SBRT for both biopsy-proven and presumed NSCLC, from 2015-2017. All patients were staged with PET-CT and reviewed at our multi-disciplinary thoracic tumor board prior to receiving SBRT. 47 patients were identified and 49 lesions were treated. 33 (70.2%) patients had biopsy proven NSCLC while 14 (29.8%) patients had presumed lung cancer determined by probabilistic modeling. 23 (69.7%) adenocarcinomas and 10 (30.3%) squamous cell carcinomas were identified. The median tumor size was 2.05 cm (range 0.80-5.50), and the median PTV volume was 29.36 cc (range 6.70-129.30). The majority of patients received 50 Gy in 5 fractions prescribed to the PTV. Established RTOG planning parameters and normal tissue constraints were utilized. The median follow-up time was 19.4 months.

Results: 49 tumors (T1=41, T2=7, and T3=1); 28 (59.6%) male and 19 (40.4%) female; median age, 79 years (range, 56-86). Median FEV1 and DLCO at enrollment were 59% (range, 30%-112%) and 57% (range, 30%-122%), respectively. At time of review, one patient had a primary tumor recurrence, and one patient had an involved lobe failure. Primary tumor control and involved lobar control rates at 18 months were both 98.0%. 3/47 (6.4%) patients experienced regional failure and 5/47 (10.6%) patients experienced local-regional failure, while 4/47 (8.5%) patients experienced disseminated failure. Disease-free and overall survival rates were 66.0% and 78.7% respectively, at a median follow-up of 19.4 months. Treatment-related grade 3 toxicity was noted in one patient (rib fracture). No grade 4 or 5 toxicities were documented.

Conclusion: We observed excellent outcomes and low Grade 3 or higher toxicities, consistent with recently published prospective data from the RTOG. The military's unique health care system with universal access to care, access to PET staging and imaging surveillance, and routine follow-up may have contributed to our outcomes. Additionally, nearly 30% of our patients lacked biopsy confirmation highlighting one difference between community practice and clinical trials. This review compares favorably to published prospective data, supporting excellent rates of local control and toxicity in the treatment of early stage NSCLC with SBRT.

Author Disclosure: M. Chamberlin: None. A.R. Horn: None. A. Reed: None.

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Withdrawn

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Treatment of T3N0 Non-Small Cell Lung Cancer with Chest Wall Invasion Using Stereotactic Body Radiotherapy



W.R. Kennedy, P. Gabani, J. Nikitas, C.G. Robinson, J.D. Bradley, and M.C. Roach, Jr; *Washington University School of Medicine, Department of Radiation Oncology, St. Louis, MO*

Purpose/Objective(s): Chest wall invasion (CWI) is seen in approximately 5% of localized non-small cell lung cancer (NSCLC). While stereotactic body radiotherapy (SBRT) is an established treatment modality for early-stage NSCLC, data on its role in the management of tumors invading the chest wall are sparse. The purpose of this study is to

investigate the safety and efficacy of SBRT in patients with T3N0 NSCLC due to CWI.

Materials/Methods: Patients with primary NSCLC invading the chest wall were identified using a prospective institutional review board-approved SBRT registry. Chest wall invasion was defined as evidence of either soft tissue invasion or bony destruction on diagnostic imaging. We excluded patients with recurrent or metastatic disease. All patients were treated with definitive SBRT. Prescribed dose was 50Gy in 5 fractions for all patients except two, who both received 54Gy in 3 fractions. Kaplan-Meier analysis was used to estimate survival outcomes.

Results: We identified 11 patients with evidence of CWI treated between 2006 and 2017. All patients had a primary T3N0 NSCLC. The median age was 68 years (range, 58 – 85), median Karnofsky performance status was 5 (range, 3 – 10). Median tumor diameter was 3.0 cm (range, 0.9 – 7.2 cm). At a median follow-up of 8.1 months (range, 2.1 – 62.5 months), 1-year primary tumor control was 88%, involved lobar control was 88%, local-regional control was 80%, distant control was 91%, and overall survival was 70%. Of the 4 patients with pre-treatment chest wall pain, 3 reported improvement after SBRT. Two patients reported new chest wall pain or worsening of pre-existing pain. No grade 3+ toxicity was reported, with 1 patient experiencing grade 1-2 skin toxicity and 3 patients experiencing grade 1-2 radiation pneumonitis.

Conclusion: Stereotactic body radiotherapy for patients with NSCLC invading the chest wall is a feasible treatment modality associated with high early tumor control rates and low treatment-related toxicity. Most patients with pre-treatment chest wall pain experienced at least partial relief after SBRT, with no grade 3+ toxicity observed. Prospective validation of SBRT in this select cohort should be pursued.

Author Disclosure: W.R. Kennedy: None. P. Gabani: None. J. Nikitas: None. C.G. Robinson: Research Grant; Varian Medical Systems, Elekta. Speaker's Bureau; Varian Medical Systems, DFINE. Advisory Board; Radialogica. Travel Expenses; Varian Medical Systems, DFINE. Stock Options; Radialogica. J.D. Bradley: Research Grant; ViewRay, Inc, Mevion Medical Systems. Travel Expenses; Mevion Medical Systems. Organize NRG Oncology research agenda on lung cancer; American College of Radiology. M.C. Roach: Travel Expenses; BTG, Varian, Elekta.

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Single-Physician Retrospective Evaluation of Stereotactic Body Radiotherapy for Non-Small-Cell Lung Cancer



E. Galvan¹ and Y. Li²; ¹UT Health San Antonio Mays Cancer Center, San Antonio, TX, ²Mays Cancer Center, UT Health San Antonio, San Antonio, TX

Purpose/Objective(s): The goal of this project is to characterize outcomes after stereotactic body radiotherapy (SBRT) to the chest in non-small-cell lung cancer (NSCLC) patients.

Materials/Methods: Retrospective analysis was performed at a single institution on 102 patients who underwent radiation therapy to the chest to 125 lesions of NSCLC, treated by a single radiation oncologist specializing in treating lung cancer. SBRT was used to treat 116 lesions.

Results: Patient follow-up available for 62 patients averaged 23.4 months (median: 15.9). Forty-five (36%) of lesions were squamous cell (SCC), 58 (46%) adenocarcinoma, 5 (4%) NSCLC not otherwise specified, and 17 (14%) lesions radiographically identified had no biopsy performed because of patients' severe medical comorbidities. SBRT-treated lesions were T1a (55), T1b (30), T2 (22), T3 (4) and T4 (1). Five patients with locally-advanced disease were first treated with 3D conformal radiation (3DCRT) or IMRT to include mediastinal lymphadenopathy (LAD), and were later treated with SBRT to second primary sites (total of 6 lesions). Twenty patients had two courses of RT, and three had a third. Three patients had synchronous primaries; 2 were treated with simultaneous SBRT and 1 with subsequent IMRT to include LAD. Two patients were treated to adjacent lobar failure after SBRT, and 2 were treated to mediastinal locoregional failure. Six patients had progressive locoregional disease (PD), diagnosed

an average of 12.6 (range: 2.4-32.2) months after SBRT. Four patients developed distant metastasis (DM), an average of 9.5 (range: 3.0-21.1) months after definitive SBRT; 3 of these patients had adenocarcinoma, and 1 had SCC. Five patients had metastatic adenocarcinoma at diagnosis (including diaphragmatic nodule, malignant pleural effusion, or DM), and have follow-up an average of 31.9 months (median: 37.5; range: 4.3-53.9) after SBRT for local control with disease otherwise controlled by novel systemic therapies (alectinib, nivolumab, pemetrexed), with no evidence of progression of the SBRT-treated lesion at follow-up; 2 of these patients are still alive on these therapies. Forty-eight of the 58 patients (83%) without DM at diagnosis and for whom follow-up data is available had no evidence of PD or DM.

Conclusion: In our experience, 83% of patients were free from locoregional recurrence or DM at follow-up after SBRT. Not all treated patients were early-stage. While SBRT is usually used to treat patients with non-operable, early-stage lung cancer, SBRT also provides local control in patients with metastatic disease at diagnosis and whose disease is controlled elsewhere with novel systemic therapies, many of which are being shown to afford our patients increased survival benefit.

Author Disclosure: E. Galvan: None. Y. Li: None.

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Practice patterns and impact of post-operative radiation therapy on overall survival after neoadjuvant chemotherapy for cN2 non-small cell lung cancer



Z.D. Horne,¹ S. Beriwal,² S. Abel,¹ A. Colonias,¹ and R.E. Wegner¹;

¹Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, ²UPMC Hillman Cancer Center, Pittsburgh, PA

Purpose/Objective(s): In patients with locally-advanced non-small cell lung cancer (NSCLC) who undergo neoadjuvant chemotherapy followed by resection, the impact of post-operative radiation therapy (PORT) is unknown.

Materials/Methods: Patients with non-metastatic cN2 NSCLC and known clinicopathologic staging who underwent neoadjuvant chemotherapy followed by surgery from 2004-2015 were identified from the National Cancer Database. Only patients with known number of dissected and positive nodes were included. Radiation therapy prior to surgery was excluded. Overall survival (OS) was compared using log-rank and Cox proportional hazards for uni- (UVA) and multivariable (MVA) analyses.

Results: We identified 1466 patients. Median follow up was 30.8 months. The median number of dissected nodes was 12 and median number of positive nodes was 2. The median positive lymph node ratio (LNR) was 14.3%, therefore a cutoff of 15% was utilized for analyses. PORT was delivered to 40.0% of patients. Median OS for the cohort was 47.4 months. Pathologic nodal downstaging was predictive for OS. PORT was delivered to 23% ypN0, 29% ypN1, and 55% ypN2 patients. Median OS for ypN0, ypN1, and ypN2 patients was 58.4, 42.8, and 40 months, respectively ($p < 0.001$). Median OS for patients with LNR 0 (ypN0), $\leq 15\%$ and $> 15\%$ was 58.4, 49, and 39.8 months, respectively ($p < 0.001$). On UVA, OS was

Factor	HR (95%CI)	P
Age	1.016 (1.008-1.024)	<0.001
Year of Dx	0.950 (0.920-0.981)	0.002
ypT0	Ref	
ypT1	NS	
ypT2	1.674 (1.108-2.528)	0.014
ypT3	2.197 (1.414-3.415)	<0.001
ypT4	NS	
Positive Margin	1.452 (1.125-1.874)	0.004
Post-operative Radiation	0.819 (0.701-0.955)	0.011
LNR = 0 (ypN0)	Ref	
LNR $\leq 15\%$	1.193 (0.965-1.476)	0.103
LNR $> 15\%$	1.515 (1.257-1.826)	<0.001

predicted by age, female gender, payer type, year of diagnosis, ypN+, LNR, cT, ypT, and ypN stages and surgical margins. On MVA including all therapeutic interventions, ypT stage, LNR, surgical margins, year of diagnosis, age, and receipt of post-operative radiation were significant for OS (Table 1). The median OS for patients with LNR $> 15\%$ who received vs did not receive post-operative radiation therapy was 45.9 vs 34.2 months, respectively ($p < 0.001$). On log-rank analysis, ypN1 patients did not derive a benefit from PORT but ypN2 patients who received PORT had median OS of 45.9 vs. 34.1 months ($p = 0.006$). ypN1 patients with LNR $> 15\%$ who received PORT had a strong trend towards improved OS: 58.1 vs 42.8 months, respectively ($p = 0.068$).

Conclusion: Patients with cN2 NSCLC who undergo neoadjuvant chemotherapy and have ypN2 disease and/or high lymph node ratio appear to benefit from post-operative radiation therapy.

Author Disclosure: Z.D. Horne: None. S. Beriwal: None. S. Abel: None. A. Colonias: None. R.E. Wegner: None.

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Role of Adjuvant Therapy in Clinically N2 Non-Small Cell Lung Cancer Patients Undergoing Neoadjuvant Chemotherapy and Surgery



A. Shinde,¹ R. Li,¹ S.M. Glaser,¹ E. Massarelli,² M. Koczywas,²

K.L. Reckamp,² R. Salgia,² and A. Amini¹; ¹Department of Radiation Oncology, City of Hope National Medical Center, Duarte, CA,

²Department of Medical Oncology, City of Hope National Medical Center, Duarte, CA

Purpose/Objective(s): Optimal adjuvant therapy in patients with clinically N2 non-small cell lung cancer (NSCLC) who undergo neoadjuvant chemotherapy followed by surgery is unknown. We evaluated the impact of adjuvant chemotherapy (CT) and external beam radiation (EBRT) in this clinical scenario.

Materials/Methods: Patients with non-metastatic NSCLC diagnosed from 2004 to 2015 were identified from the National Cancer Database. Patients with clinical N2 disease who underwent induction chemotherapy followed by surgery were included. Patients were excluded if they received EBRT prior to surgery. A six-month landmark analysis was performed to allow for completion of all planned therapy. Overall survival (OS) was compared using log-rank Kaplan-Meier (KM) for univariate analysis (UVA), and Cox proportional hazards for multivariate analysis (MVA). Logistic regression was used to determine predictors of chemotherapy utilization. Subset analysis was performed for patients based on post-chemotherapy pathologic nodal stage (ypN).

Results: We identified 2086 patients. Median follow-up was 32 months, 46 months for survivors. Patients received adjuvant CT and EBRT in 18.4% and 34.1% of cases, respectively. On UVA for the entire cohort, adjuvant CT correlated with improved OS (3-year OS 60.5% vs 54.7%, $p = 0.014$); there was no OS benefit with adjuvant EBRT. On subset analysis, stratification by ypN showed no significant benefit in N0 or N1 patients to CT or EBRT. CT demonstrated an OS benefit for N2 patients (3-year OS 57.0% vs 47.7%, $p = 0.002$). On further analysis, the benefit of EBRT for ypN2 were only for those who did not receive adjuvant CT (3-year OS 50.5% vs 45.6%, $p = 0.047$). Factors that predicted for utilization of adjuvant CT included more recent year of diagnosis, higher ypN, and use of adjuvant EBRT. On MVA for the entire cohort, increasing pathologic T stage (ypT), ypN, positive margin, and sublobar resection worsened OS ($p < 0.05$ for all). Treatment after 2009, female gender, other (including asian) race, private insurance had improved OS ($p < 0.05$ for all). Receipt of adjuvant chemotherapy improved OS (HR 0.77, $p = 0.002$). Receipt of adjuvant RT did not affect survival (HR 1.01, $p = 0.88$). On MVA stratified by ypN, there was no survival benefit to adjuvant CT or EBRT for ypN0 or ypN1 patients. For ypN2 patients, the addition of adjuvant CT improved OS (HR 0.75, $p = 0.007$), while EBRT did not (HR 0.90, $p = 0.24$).

Conclusion: For patients who receive neoadjuvant CT (without radiation) followed by surgery, use of adjuvant CT is associated with improved OS, primarily in those with residual ypN2 disease. Adjuvant EBRT may only provide a survival benefit in ypN2 patients that are not candidates for

additional systemic treatment. Patients with ypN0 or ypN1 disease do not seem to benefit from adjuvant therapy.

Author Disclosure: A. Shinde: None. R. Li: None. S.M. Glaser: None. E. Massarelli: None. M. Koczywas: None. K.L. Reckamp: None. R. Salgia: None. A. Amiri: None.

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Definitive Radiotherapy for Inoperable Stage IIB Non-Small Cell Lung Cancer: Patterns of Care and Comparative Effectiveness Analyses Using the National Cancer Database



C.D. Jacobs,¹ J. Gao,² X. Wang,² N.E. Ready,³ J. Clarke,³ B. Tong,⁴ C.R. Kelsey,¹ G. Suneja,¹ and J.A. Torok, Jr.¹; ¹Duke University, Department of Radiation Oncology, Durham, NC, ²Duke University, Department of Biostatistics and Bioinformatics, Durham, NC, ³Duke University, Department of Medical Oncology, Durham, NC, ⁴Duke University, Department of Surgery, Durham, NC

Purpose/Objective(s): Stereotactic body radiotherapy (SBRT) and concurrent chemoradiation are established standards for inoperable stage I and III non-small cell lung cancer (NSCLC), respectively. In contrast, optimal definitive radiotherapy (RT) for inoperable stage IIB (T3N0M0 or T1-2N1M0) NSCLC is less defined. Patterns of care and survival analyses for stage IIB NSCLC treated non-surgically were performed.

Materials/Methods: All adult subjects diagnosed with T3N0M0 or T1-2N1M0 NSCLC between 2004-2015 in the National Cancer Database (NCDB) were identified. All reasons for T3 based on AJCC 7th edition (size, invasion, obstruction, and multifocal in the same lobe) were included. Based on fraction (fx) size and number, RT groups were defined as SBRT (1-5 fx of ≥ 10 Gy/fx), hypofractionated RT (HFRT, 6-35 fx of > 2 Gy/fx), and conventionally fractionated RT (CFRT, 25-41 fx of 1.8-2 Gy/fx). Exclusion criteria include surgery, no RT, RT to non-thoracic site, SBRT dose < 30 Gy or > 60 Gy, and HFRT/CFRT dose < 50 Gy or > 74 Gy. RT groups were stratified by use of systemic therapy (ST). Demographic, tumor, and treatment characteristics among the different RT groups were compared using Chi-squared and Kruskal-Wallis tests for categorical and continuous variables, respectively. Overall survival (OS) of the RT groups was compared with the log-rank test.

Results: Among 9279 subjects with stage IIB NSCLC, trends in proportional utilization between 2004-2009 vs 2010-2015 were 3.3% vs 16.1% (12.9% net increase) for SBRT, 13.0% vs 14.6% (1.6% net increase) for HFRT, and 83.8% vs 69.2% (14.6% net decrease) for CFRT. Differences between RT groups are summarized in the table.

	T3N0M0 NSCLC			p-value	T1-2N1M0 NSCLC		p-value
	SBRT (n = 883)	HFRT (n = 471)	CFRT (n = 3023)		HFRT (n = 370)	CFRT (n = 4532)	
Age (years), median	74	76	71	<0.001	77	72	<0.001
Sex (female)	54%	43%	41%	<0.001	44%	45%	0.654
Charlson-Deyo ≥ 2	17%	18%	14%	0.069	17%	16%	0.204
Prior malignancy	43%	30%	23%	<0.001	33%	27%	0.022
Tumor size (cm), median	2.5	4.3	5.0	<0.001	3.7	3.7	0.445
Multifocal in same lobe	69%	29%	14%	<0.001	NA	NA	NA
Histology (squamous cell)	50%	64%	66%	<0.001	60%	60%	0.5650
Use of ST	9%	26%	77%	<0.001	32%	75%	<0.001
Biologically effective dose (Gy ₁₀), median	105.6	75.0	78.6	<0.001	75.0	78.4	0.6329

In the T3N0M0 cohort, median OS was 26.8, 15.7, and 20.8 months for SBRT, HFRT, and CFRT, respectively ($p < 0.001$). In the T1-2N1M0 cohort, median OS was 16.4, 17.2, 20.0, and 23.9 months for HFRT alone, CFRT alone, HFRT+ST, and CFRT+ST, respectively ($p < 0.001$).

Conclusion: CFRT+ST is the most frequently used method to treat stage IIB NSCLC in the U.S. when surgery is not performed, though it is decreasing. Use of SBRT for T3N0M0 NSCLC is increasing most rapidly, and SBRT was associated with improved OS, although patient selection may have contributed to improved outcome.

Author Disclosure: C.D. Jacobs: None. J. Gao: None. X. Wang: None. N.E. Ready: Advisory Board; BMS, Merck, Celgene, Novartis, Abbvie, AstraZeneca. J. Clarke: Research Grant; Bristol-Myers Squibb, Medpacto. Speaker's Bureau; Merck, Guardant. B. Tong: Speaker's Bureau; Integra Life Sciences. Advisory Board; Medtronic. C.R. Kelsey: None. G. Suneja: None. J.A. Torok: None.

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Short-Term Mortality Associated with Definitive Chemoradiotherapy Versus Trimodality Therapy for Locally Advanced Non-Small Cell Lung Cancer



V. Verma,¹ W. Haque,² E.B. Butler,² B.S. Teh,³ and C.G. Rusthoven, Jr.⁴; ¹Department of Radiation Oncology, Nebraska, Pittsburgh, PA, ²Department of Radiation Oncology, Houston Methodist Hospital, Houston, TX, ³Houston Methodist Hospital, Houston, TX, ⁴Department of Radiation Oncology, University of Colorado Denver, Aurora, CO

Purpose/Objective(s): Management of locally advanced non-small cell lung cancer (NSCLC) is highly controversial but is commonly performed with definitive chemoradiation (dCRT) or neoadjuvant chemoradiation and surgery (nCRT+S). Because comparative investigations of short-term mortality following trimodality versus bimodality approaches are lacking, we addressed this knowledge gap by exploring 30- and 90-day mortality between nCRT+S and dCRT for these patients.

Materials/Methods: The National Cancer Database was queried (2004-2014) for T1-3N2 or T3-4N0-1 (except T3N0) NSCLC that received nCRT+S or dCRT. Statistics included cumulative incidence analysis of 30- and 90-day mortality (before and following propensity score matching) and Cox regression to evaluate predictors thereof.

Results: Of 28,379 patients, 4,063 (14.3%) underwent nCRT-S, and 24,316 (85.6%) dCRT. Of the trimodality patients, 79.2% received lobectomy, 8.2% sublobar resection, and 12.5% pneumonectomy. In addition to age, several sociodemographic and oncologic variables were associated with 30- and 90-day mortality, along with trimodality therapy. Thirty-day (3.4% vs. 0.8%, $p < 0.001$) and 90-day (7.5% vs. 6.6%, $p = 0.017$) mortality was higher with nCRT+S, which persisted following propensity matching (3.4% vs. 0.4% and 7.5% vs. 5.3% respectively, both $p < 0.001$). At both 30 and 90 days, pneumonectomy was associated with higher mortality than lobectomy (6.1% vs. 2.9% and 11.1% vs. 6.9% respectively, both $p < 0.001$). When subdividing based on age, trimodality management was associated with statistically higher mortality in patients aged 66-80, but not ≤ 65 .

Conclusion: Treatment with nCRT+S was associated with greater 30- and 90- day post-treatment mortality when compared to treatment with dCRT, with larger differences observed in 30-day post-treatment mortality. Comparatively characterizing short-term mortality following dCRT versus nCRT+S may better inform shared decision-making between patients and providers when weighing both options for locally advanced NSCLC.

Author Disclosure: V. Verma: None. W. Haque: None. E. Butler: None. B.S. Teh: None. C.G. Rusthoven: Honoraria; Takeda Pharmaceuticals, US Oncology.

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Systemic Therapy as a Prognosticator in Patients Receiving Stereotactic Radiosurgery for Non-Small Cell Lung Cancer



N. Wandrey, J. Pawlowski, F. Seddo, R.L. Crownover, and M. Fakhreddine; Mays Cancer Center, UT Health San Antonio, San Antonio, TX

Purpose/Objective(s): Brain metastases (BM) frequently occur in patients with lung cancer and are associated with a poor prognosis. Stereotactic radiosurgery (SRS) offers an alternative in treatment of BM with less neurocognitive decline compared with whole brain radiation (WBRT). In addition, immunotherapy (IT) has significantly altered the treatment landscape of patients with metastatic lung cancer by increasing overall survival (OS). These novel treatments have redefined prognosis for lung cancer patients with BM. The purpose of our study is to determine how administration of systemic therapy, including IT, affects OS in patients who have received SRS. This information could serve as a potential modifier of prognostication tools such as brain metastases graded prognostic assessment (GPA) to select those with BM who are most likely to benefit from SRS.

Materials/Methods: Patients were identified from the National Cancer Database (NCDB) that were diagnosed from 2004-2014 with metastatic disease from a lung cancer primary that received SRS. Kaplan-Meier curves were generated to plot OS. Univariate analysis (UVA) was performed with the long-rank and Wilcoxon tests for significance. Analyzed variables included age, grade, Charles Deyo score, race, gender, nodal status, and systemic therapy. Treatment was classified as either: chemo, IT +/- chemo, and no therapy. A multivariate analysis (MVA) was performed for the same variables.

Results: 2,350 patients received SRS for BM from lung cancer primary. Of these, 1,173 patients received only chemo, 89 patients received IT +/- chemo, and 1,088 patients received no systemic therapy with SRS. The median OS was 12.9 months with chemo (95% CI 12.6 – 13.3), 17.4 months with IT +/- chemo (95% CI 15.9 – 19.0), and 9.5 months for those who received no systemic therapy with SRS (95% CI 9.1 – 9.8), $p < 0.0001$. On UVA, increasing age, increasing Charles Deyo score, increasing grade, increasing nodal stage, squamous histology, and male gender were all significantly associated with worse OS. On MVA, each of these remained statistically significant predictors of OS. Compared to chemo, IT +/- chemo was associated with a significantly improved relative risk of death (RR 0.81, $p = 0.0037$). Compared to no systemic therapy, IT +/- chemo was associated with a significantly improved relative risk of death (RR 0.65, $p < 0.0001$).

Conclusion: Lung cancer patients with BM that receive IT +/- chemo have a greater OS compared to those who received only chemo or no systemic therapy with SRS. Given this improvement in survival, patients with BM from a lung cancer primary who receive IT may be especially likely to benefit from the diminished long-term side effect profile of SRS compared to WBRT. In addition, prognostication tools such as the brain metastases GPA should take into account the notably higher survival in patients who receive IT.

Author Disclosure: N. Wandrey: None. J. Pawlowski: None. F. Seddo: None. R.L. Crownover: None. M. Fakhreddine: None.

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Overall Survival According to Systemic and Radiation Treatment Approaches in Metastatic Non-Small-Cell Lung Cancer: A National Cancer Database Analysis



C.C. Foster,¹ D.J. Sher,² C.G. Rusthoven, Jr.,³ V. Verma,⁴ M.T. Spiotto,^{1,5} R.R. Weichselbaum,¹ and M. Koshy^{1,5}; ¹Department of Radiation and Cellular Oncology, The University of Chicago Medicine, Chicago, IL, ²Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX, ³Department of Radiation Oncology, University of Colorado Denver, Aurora, CO, ⁴Department of Radiation Oncology, University of Nebraska Medical Center, Omaha, NE, ⁵Department of Radiation Oncology, University of Illinois Hospital and Health Sciences System, Chicago, IL

Purpose/Objective(s): Pre-clinical studies suggest enhanced anti-tumor activity by combining radiation (RT) and immunotherapy. We hypothesized that patients with stage IV non-small-cell lung cancer (NSCLC) receiving RT and immunotherapy would have improved overall survival (OS) compared to those receiving immunotherapy or chemotherapy alone. Additionally, we investigated the influence of RT technique on OS for patients receiving RT and immunotherapy.

Materials/Methods: The National Cancer Database was queried for patients diagnosed with stage IV NSCLC from 2013-2014 who received chemotherapy or immunotherapy. Patients were further classified as receiving conventionally fractionated palliative RT or stereotactic body radiotherapy (SBRT). The Kaplan-Meier method and log-rank test were used for univariate OS analyses, and Cox proportional hazards models were used for multivariate OS analyses.

Results: In total, 44,498 patients were included with 13% receiving immunotherapy, 46.8% receiving palliative RT, and 4.7% receiving SBRT. On multivariate analysis, immunotherapy (hazard ratio [HR]:0.81, 95% confidence interval [CI]:0.78-0.83) and SBRT (HR:0.78, 95%CI:0.70-0.78) both independently associated with improved OS compared to patients receiving chemotherapy and no RT, respectively; however, the interaction term for SBRT and immunotherapy did not reach significance ($p = 0.89$). In the immunotherapy subset ($n = 5,807$), median OS for no RT, palliative RT, and SBRT was 14.5, 10.9, and 18.2 months, respectively ($p < 0.001$) with palliative RT (HR:1.37, 95%CI:1.29-1.46) and SBRT (HR:0.78, 95%CI:0.66-0.93) independently associating with OS on multivariate analysis. In the SBRT subset ($n = 2,084$), median OS was 18.2 months for immunotherapy and 14.3 months for chemotherapy ($p = 0.004$) with immunotherapy (HR:0.82, 95%CI:0.69-0.98) associating with improved OS on multivariate analysis.

Conclusion: Treatment with SBRT was associated with improved OS in patients with metastatic NSCLC, irrespective of whether the systemic treatment was cytotoxic chemotherapy or immunotherapy. While there was no statistical support for additional synergy between SBRT and immunotherapy, the particularly impressive survival in this cohort strongly argues for evaluation in prospective randomized trials.

Author Disclosure: C.C. Foster: None. D.J. Sher: None. C.G. Rusthoven: None. V. Verma: None. M.T. Spiotto: None. R.R. Weichselbaum: None. M. Koshy: None.

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Safety and Efficacy of Lung Stereotactic Body Radiation Therapy for Surgical Staple Line Recurrences



J.F. Drogos,¹ S. Mayekar,² G. Tolekidis,¹ and G. Marwaha³; ¹Rush University Medical Center, Chicago, IL, ²University of Pennsylvania, Philadelphia, PA, ³Rush Medical Center, Chicago, IL

Purpose/Objective(s): Surgical resection remains the gold standard for stage I non-small cell lung cancer (NSCLC) and is often employed for the diagnostic/therapeutic management of solitary metastases. Despite the low incidence of local recurrences (LR) along surgical staple lines, the ideal strategy for managing tumor recurrences of the staple lines have not been well established. We update our initial report on the safety and efficacy of lung SBRT as a single modality salvage treatment strategy for staple line recurrences following surgical resection.

Materials/Methods: We identified 15 patients from an IRB-approved prospectively maintained database who were treated for staple line recurrences after surgical resection for the management of stage I NSCLC or oligometastases. These patients were treated from 5/2012 to 6/2018. Ten patients had a primary, NSCLC and five patients had oligometastases. We calculated the median time from surgery to SBRT treatment, median follow up (MFU), and crude rates of local (defined as in-field and along the staple line), regional (defined as out-of-field lobe/lung and/or regional lymph nodes), and distant (contralateral thorax or distant systemic spread) control. Dosimetric information including Planning Treatment Volume (cc), total radiation dose, dose per fraction and SBRT treatment planning techniques were also evaluated. Common terminology criteria for adverse events version 4 (CTCAEv4) were used to measure treatment-related toxicities.

Results: Median age at the time of treatment was 67 years (range 50-86 years). The median time from LR to initiation of SBRT was 17 months (range 3-75 months). The median total SBRT dose was 54 Gy (range 45.0-60.0 Gy) with median dose per fraction of 11.50 Gy (range 4.5-18.0 Gy). A simultaneous integrated boost (SIB) technique, which included the entire staple line with a tumor boost, was employed in 4/15 (27%) cases. The

median PTV for all patients was 17.90 cc (range 9.40-47.10 cc). The median combined PTV of patients treated with an SIB technique including the staple line was 22.02 cc (range 15.43-29.08 cc). With MFU of 22 months (range 2-67 months) one patient (6.7%) experienced a local failure at the staple line, for a crude local control rate of 93.3%. Three patients with NSCLC (20.0%), including the one local failure, failed regionally (in the lung, outside of the SBRT field) and distantly at 8, 9 and 36 months respectively. Of the 12 patients (75%) with toxicity data available, only grade 1 toxicities were reported (fatigue (1), dyspnea (1), pneumonitis (2), or chest wall pain (1)).

Conclusion: Salvage SBRT for surgical staple line failures appears to be very efficacious and well tolerated (no grade 2 or above toxicities). Further investigation is needed to determine the optimal dose and treatment volume for this unique, but growing cohort of patients.

Author Disclosure: **J. Drogos:** None. **S. Mayekar:** None. **G. Tolekidis:** None. **G. Marwaha:** None.

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Tumor Treating Fields and radiosurgery for supra- and/or infratentorial brain metastases (1-10) from NSCLC in the phase 3 METIS study



M.P. Mehta,¹ V. Gondi,² M. Ahluwalia,³ and P.D. Brown⁴; ¹Miami Cancer Institute, Miami, FL, ²Northwestern Medicine Chicago Proton Center and Northwestern Medicine Cancer Center Warrenville, Warrenville, IL, ³Department of Medical Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, ⁴Dept. of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Purpose/Objective(s): Tumor Treating Fields (TTFields) are non-invasive, loco-regional, anti-mitotic treatment modality comprising low intensity alternating electric fields. TTFields has demonstrated efficacy in non-small cell lung cancer (NSCLC) in *in vitro* and *in vivo* models, and in a phase I/II clinical study. TTFields treatment to the brain had a favorable toxicity profile and extended overall survival in newly-diagnosed glioblastoma. This prospective, multicenter study [NCT02831959] investigates the efficacy, safety and neurocognitive outcomes of TTFields in NSCLC patients with brain metastases.

Materials/Methods: NSCLC patients (N=270) with 1-10 brain metastases are treated with stereotactic radio-surgery (SRS) and randomized 1:1 to continuous TTFields (150 kHz, > 18 hours/day) within 7 days of SRS or supportive care following the SRS. The TTFields portable device delivers TTFields to the brain using 4 transducer arrays and allows normal daily activities. Patients receive the best standard-of-care for their systemic disease. Patients are followed every two months until second intracranial progression. Patients in the control arm are allowed to cross over to TTFields arm at the time of second intracranial progression. Key inclusion criteria: KPS \geq 70, new diagnosis of 1 inoperable or 2-10 supra- and/or infratentorial brain metastases from NSCLC amenable to SRS, KPS \geq 70, at least one brain metastases 1 cm or larger, and optimal therapy for extracranial disease. Prior WBRT, a single resectable lesion or recurrent brain metastases are exclusionary. Primary endpoint is time to 1st intracranial progression. Secondary endpoints include time to neurocognitive failure, overall survival, radiological response rate (RANO-BM and RECIST V1.1); quality-of-life; adverse events; time to first/second intracranial progression for patients with 1-4 and 5-10 brain metastases; bi-monthly intracranial progression rate from 2-12 months; and time to second intracranial and distant progression. The sample size (N=270) was calculated using a log-rank test (Lakatos 1988 and 2002) with 80% power at a two-sided alpha of 0.05 to detect a hazard ratio of 0.57.

Results: n/a TiP.

Conclusion: n/a TiP.

Author Disclosure: **M.P. Mehta:** Personal fees; Novelos. Personal fees; Novocure, Abbott, BMS, Novartis, Pharmacyclics. **V. Gondi:** Partner; Radiation Oncology Consultants, Ltd. Partnership; Radiation Oncology Consultants, Ltd. Co-Principal Investigator; NRG Oncology. **M. Ahluwalia:** Research Grant; Novartis, Novocure. Consultant; Incyte, Monteris

Medical Inc; American Society of Clinical Oncology, Society of Neuro-Oncology. **P.D. Brown:** Honoraria; UpToDate, Novella DSMB.

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Computational simulations for investigating the efficacy and safety of tumor treating fields delivered to the thorax



U. Weinberg,¹ H.S. Hershkovich,¹ E. Kirson,² and Z. Bomzon²; ¹Novocure, Haifa, Israel, ²Novocure Ltd, Haifa, Israel

Purpose/Objective(s): Tumor Treating Fields (TTFields) are an anti-mitotic therapy utilizing low intensity, alternating electric fields in the intermediate frequency, and are FDA approved for the treatment of glioblastoma. The STELLAR phase 2 registration trial recently demonstrated a significant extension in median overall survival among mesothelioma patients treated with Tumor Treating Fields plus standard of care chemotherapy compared to historical control data of patients who received standard of care chemotherapy alone. The results of this trial point at the potential benefit of TTFields when treating cancer located in the thorax.

Preclinical studies suggest that treatment efficacy increases with the intensity of the electric field. Therefore, optimizing treatment requires a deep understanding of how TTFields distribute within the body. In addition, simulations can be used to evaluate the safety of the treatment by assessing tissue heating associated with absorption of the electric field. Here we present a simulation-based study investigating the field distribution and associated heating in male and female realistic computational phantoms when delivering TTFields to the thorax

Materials/Methods: Delivery of TTFields to the thorax of realistic computational phantoms of a male, female and obese male (ZMT, Zurich, Switzerland) were performed. The field was delivered to the computational phantoms using transducer arrays with characteristics similar to those used to deliver TTFields to the thorax with the NovoTTF-100L. The field intensities within the lungs of the models were then evaluated. In addition, Specific Absorption Rate (SAR), a metric for assessing heating due to electromagnetic absorption, was calculated.

Results: The highest field intensities within the lungs were obtained when the arrays were axially-aligned with the parenchyma as much as anatomically possible. Under these conditions, field intensities throughout the lungs exceeded the therapeutic threshold of 1 V/cm in all models. Within the internal organs, SAR values were generally below the allowed level of 10 W/kg set out in the ICNIRP guidelines for occupational exposure [1], with maximum SAR levels not exceeding 20 W/kg. Occupational exposure standards typically incorporate a safety factor of around 10 when setting basic restrictions, therefore this level of SAR is considered safe and unlikely to lead to heat-related tissue damage.

Conclusion: This study shows that TTFields can be delivered to the lungs at therapeutic levels, and that the therapy is highly unlikely to cause damage through tissue heating.

References

1. ICNIRP guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz), Published in Health Physics 74 (4) 494-522; 1998

Author Disclosure: **U. Weinberg:** Stock; Novocure. **H.S. Hershkovich:** Stock; Novocure. **E. Kirson:** Stock; Novocure. chief science officer; Novocure. **Z. Bomzon:** Stock; Novocure.

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Tumor Treating Fields concurrent with standard of care treatment for stage 4 non-small cell lung cancer (NSCLC) following platinum failure: Phase 3 LUNAR study



U. Weinberg, O. Farber, M. Giladi, Z. Bomzon, and E. Kirson; Novocure Ltd, Haifa, Israel

Purpose/Objective(s): Tumor Treating Fields (TTFields) is a non-invasive, anti-mitotic treatment that disrupts the formation of the mitotic

spindle and dislocation of intracellular constituents. TTFields plus temozolomide significantly extended survival in newly diagnosed glioblastoma. Efficacy of TTFields in NSCLC has been shown in preclinical *in vitro* and *in vivo* models. TTFields demonstrated safety in a phase I/III pilot study with pemetrexed. We hypothesize that adding TTFields to immune checkpoint inhibitors or docetaxel following platinum doublet failure will increase overall survival (OS).

Materials/Methods: Patients (N=534), with squamous or non-squamous NSCLC, are stratified by their selected standard therapy (immune checkpoint inhibitors or docetaxel), histology (squamous vs. non-squamous) and geographical region. Key inclusion criteria are disease progression while on or after platinum-based therapy, ECOG 0-2, no electronic medical devices in the upper torso, and absence of brain metastasis. Docetaxel or immune checkpoint inhibitors are given at standard doses. TTFields are applied to the upper torso for ≥ 18 hours/day, allowing patients to maintain daily activities. TTFields are continued until progression in the thorax and/or liver. Follow up is performed once q6 weeks, including CT scans of the chest and abdomen. On progression in the thorax and/or liver, patients have 3 post-progression follow up visits and are then followed monthly for survival. The primary endpoint is superiority in OS between patients treated with TTFields in combination with the standard of care treatments versus standard of care treatments alone. Key secondary endpoints compare the OS in patients treated with TTFields and docetaxel versus docetaxel alone, and patients treated with TTFields and immune checkpoint inhibitors vs those treated with immune checkpoint inhibitors alone. An exploratory analysis will test non-inferiority of TTFields with docetaxel compared to checkpoint inhibitors alone. Secondary endpoints include progression-free survival, radiological response rate, quality of life based on the EORTC QLQ C30 questionnaire and severity and frequency of adverse events. The sample size is powered to detect a HR of 0.75 in TTFields-treated patients versus control group.

Results: n/a TiP.

Conclusion: n/a TiP.

Author Disclosure: **U. Weinberg:** Stock Options; Novocure. **O. Farber:** Stock Options; Novocure. **M. Giladi:** Stock Options; Novocure. **Z. Bomzon:** Stock Options; Novocure. **E. Kirson:** Stock Options; Novocure.

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Outcomes and Quality Measures Among Homeless Lung Cancer Patients in A Single Institution.



K. Concannon,¹ H. Linden,¹ H. Thayer,¹ and C. Baik²; ¹University of Washington, Seattle, WA, ²University of Washington/Seattle Cancer Care Alliance, Seattle, WA

Purpose/Objective(s): Lung cancer remains the leading cause of cancer death in the US. Contributing to the limited improvement in overall lung cancer mortality is the presence of poorer outcomes among vulnerable populations such as the homeless. It has not yet been described how barriers associated with homelessness affect their healthcare. We hypothesized that homeless patients experience lower rates of appointment adherence as our primary endpoint; delays in biopsy after imaging, increased rates of ER visits and inpatient stays, and overall mortality as secondary endpoints.

Materials/Methods: To investigate this, we conducted a retrospective review of all lung cancer patients with non-small cell carcinoma (N=82) with appointments made between 9/2012 and 9/2017 at an academic county hospital with a dedication to homeless health in a major US city. Data were collected from electronic medical records manually and analyzed using ANOVA for continuous variables or Pearson's Chi-squared for categorical data.

Results: Of the 82 patients treated for non-small cell lung cancer, 14 (17%) were homeless at the time of their treatment. Once a diagnosis was achieved, homeless patients missed a mean of 25.3% of appointments as compared to 15% of appointments among non-homeless patients (p=0.028). Among homeless patients the mean time from radiographic evidence of malignancy to biopsy was 173 days as compared to 51 days among housed patients (p-value=0.009). The average number of ER

visits, hospital admissions, and inpatient stays after diagnosis among homeless and housed patients were 2.3 and 2.5 (p-value=0.83), 1.4 and 1.5 (p=0.95), and 11.8 and 8.0 (p=0.39).

Conclusion: We observed that homeless patients experience delays in diagnosis and miss more appointments than housed patients and delays in biopsy after radiographic evidence of malignancy. In this small retrospective analysis, we were unable to conclude that this impacts ER visits, hospital length of stay, or overall mortality. Our findings suggest that the support system for these patients needs improvement if we aim to offer them the same high-level care offered to housed patients. Homeless patients also experience delays in diagnosis after radiographic concerns which suggests there is a palpable impact from their decreased access to care. Limitations to this study include a small sample size, potential contribution of other comorbidities, and an inability to determine why patients miss appointments. This is a single institutional experience, in an academic county hospital serving as a safety net for patients suffering from social barriers to health and is inherently not generalizable to other academic institutions.

Author Disclosure: **K. Concannon:** None. **H. Linden:** None. **H. Thayer:** None. **C. Baik:** AstraZeneca.

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Withdrawn

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Factors Associated with No Treatment in Stage I Non-Small Cell Lung Cancer



S.M. Dalwadi,¹ E.B. Butler,² B.S. Teh,³ and A.M. Farach²; ¹Baylor College of Medicine, Houston, TX, ²Department of Radiation Oncology, Houston Methodist Hospital, Houston, TX, ³Houston Methodist Hospital, Houston, TX

Purpose/Objective(s): In the era of SBRT, definitive therapy for stage I NSCLC is extended to nonsurgical candidates. Early data suggests local control and survival outcomes comparable to surgery. Despite this, a proportion of stage I NSCLC patients in the US population remain untreated. We aim to identify factors associated with lack of treatment in stage I NSCLC.

Materials/Methods: Using SEER, 62,213 stage I NSCLC cases diagnosed between 2004-2012 were identified. Patient characteristics were compared using Chi squared test. Multivariate analysis for no treatment was performed using Kaplan Meyer actuarial method and COX proportional hazard ratio.

Results: 11.9% of patients (n=7373) in this dataset did not receive treatment for T1 or T2N0 NSCLC. Lack of insurance, single or widowed marital status, advancing age, multiple primary malignancies, lower income, black or American Indian race, and male sex all contributed to lower likelihood of receiving treatment on multivariable analysis (all p<0.0001). Lack of treatment portends a significantly worse cancer-specific (20% vs 66% at 5Y, p<0.0001) and overall survival (10% vs 50% at 5Y, p<0.0001).

Conclusion: Many socioeconomic factors contribute to lack of treatment in stage I NSCLC and addressing these disparities is crucial. While some patients with competing comorbidities are appropriately forgoing treatment, others may benefit from the minimally-invasive treatment modalities available.

Author Disclosure: **S.M. Dalwadi:** None. **E. Butler:** None. **B.S. Teh:** None. **A.M. Farach:** None.

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Lessons derived from A Prospective *In-Silico* Quality Assurance Study of Contouring Target Volumes within a Cooperative Group Setting: Insights from Radiation Oncologists' Perspective



H. Elhalawani,¹ F. Laurie,² K. Ulin,³ L.A. Kachnic,⁴ C.D. Fuller,⁵ and C.R. Thomas, Jr⁶; ¹Department of Radiation Oncology, University of

Texas MD Anderson Cancer Center, Houston, TX, ²IROC Rhode Island (QARC), Lincoln, RI, ³University of Massachusetts Memorial Medical Center, Worcester, MA, United States, ⁴Vanderbilt Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN, ⁵University of Texas Graduate School of Biomedical Sciences, Houston, TX, ⁶Department of Radiation Oncology, Oregon Health and Science University, Portland, OR

Purpose/Objective(s): Target delineation variability is a significant technical impediment in cooperative group trials which employ IMRT and may impact outcome. The SWOG Radiation Oncology Committee conducted a prospective *in-silico* quality assurance pilot study based on the hypothesis that it is feasible to determine how diverse institutions participating in clinical trials are incorporating FDG PET-CT, 3D-, and 4D-CT data in RT planning.

Materials/Methods: CT simulation scans were acquired from four patients with superior sulcus tumors. Two patients had both simulation 4D-CT and FDG-PET-CT while two patients had 3D-CT and FDG-PET-CT. Seventeen radiation oncologists independently delineated treatment target volumes (TVs). These included gross primary and nodal tumor volumes (GTV_P and GTV_N, respectively) as well as clinical and planning target volumes. Six board-certified thoracic radiation oncologists were designated as the 'Expert observers' for this study. Their delineations were used to create a simultaneous truth and performance level estimation (STAPLE) contours using commercial software. Individual observer contours were then compared to expert's STAPLE contours using similarity evaluation metrics. After plan completion, each user was asked to fill out an online survey assessing subjective responses to contouring tasks. It included categorical Likert scale evaluation of institutional practices, and subjective observers' feedback. One-way analysis of variance (ANOVA) was applied to assess statistically significant differences among the mean values of evaluation metrics per target volume based on different participant-related variables.

Results: Seventeen radiation oncology observers (physicians), with median career experience of 11 years (IQR: 2.5-18.75). The feedback from 13 respondents to survey questions are tabulated in **Table 1**. Subgroup analysis based on our objective definition of expertise showed some similarity indices to be significantly better for the 'Expert' versus 'non-expert' groups with regards to contouring all TVs except GTVp; contrary to more subjective participant-derived feedback. There were no significant differences in all evaluation metrics for all TVs for cases with 4D-CT versus cases with 3D-CT simulation scans.

Conclusion: A prospective *in-silico* exercise for TV delineation is feasible and may warrant including as part of the pre-enrollment credentialing process for the next intergroup combined modality trial for superior sulcus lung tumors.

Table 1 Responses of the participants to the survey questions

Variable	N (%)
Thoracic radiation oncology subspecialty	
Expert	5 (38.5)
Non-expert	8 (61.5)
Time spent on contouring task (in minutes); median (IQR)	120 (42.5-150)
Treatment planning system used	
Eclipse	4 (30.8)
Focal	1 (7.7)
MIM Vista	1 (7.7)
Pinnacle	7 (7 (53.8))

Author Disclosure: **H. Elhalawani:** Employee; MD Anderson Cancer Center. **F. Laurie:** None. **K. Ulin:** None. **L.A. Kachnic:** Research Grant; NCI NCORP, SWOG. Honoraria; Up-to-Date. President; ABR. **C.D. Fuller:** Research Grant; National Institutes of Health, National Science Foundation, Elekta AB, National Institutes of Health. Grant funding; Elekta AB. Honoraria; Nederlandse Organisatie voor Wetenschappelijk Onderzoek. Consultant; Elekta AB, Nederlandse Organisatie voor Wetenschappelijk Onderzoek. Travel Expenses; Elekta AB, Nederlandse Organisatie voor Wetenschappelijk Onderzoek. **C.R. Thomas:** None.

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Improving Treatment Experience for Nunavut Patients with Lung Cancer



L.G. Kirk,¹ A. Hammond,² A. Nwafor,¹ K. Dennis,³ and M.N. Reaume⁴;
¹Ottawa Hospital Research Institute, Ottawa, ON, Canada, ²Ottawa-Baffin Nunavut Health Services, Ottawa, ON, Canada, ³The Ottawa Hospital Cancer Centre, Ottawa, ON, Canada, ⁴University of Ottawa, Ottawa, ON, Canada

Purpose/Objective(s): Inuit individuals with lung cancer from Nunavut, Canada, must seek out-of-province healthcare for cancer treatment, often travelling thousands of kilometers. Quality of life during healthcare management of advanced cancer is under-researched in this population. No data exist on how many Nunavut patients receiving palliative cancer treatments return home during their treatment. Our objective was to provide Nunavut patients better contextual information for informed consent for the treatment of metastatic lung cancer. We performed a retrospective chart review to explore travel patterns during systemic therapy.

Materials/Methods: We identified 124 patients from Nunavut diagnosed with palliative lung cancer (stage III/IV or recurrent) from January 2005 to December 2014. Lack of palliative systemic treatment excluded 77 patients. Another 7 lacked travel information. Forty patients were therefore included in the final analysis. The primary outcome was the proportion of patients who travelled to their home communities during palliative systemic treatment. The small cohort restricts this study to a descriptive review.

Results: Sixty-two percent were male. The mean age was 78 years (range 42-78). Stage III&IV and recurrent were 87% and 19% respectively. The median number of cycles of first line chemotherapy was 3 (range 1-8). Sixty percent (24 patients) never returned home during first line therapy, of which 25% (10) died prior to cycle 3. Over the 10-year study timeframe, 50% (20) of 40 patients on palliative systemic treatment returned to their community at least once during their course of treatment.

Conclusion: Our data indicate a large proportion of patients were unable to return to their home communities during the full course of palliative systemic treatment. Patient intent to travel is not documented in physician charts, as such if patients in the cohort chose to stay at our institution they were grouped as having missed opportunities to travel home. Clinicians may find our results useful to assist in selecting appropriate treatment regimens to facilitate travel and to provide context-appropriate informed consent for Nunavut patients.

Author Disclosure: **L.G. Kirk:** Research Grant; Lung Cancer Canada. **A. Hammond:** None. **A. Nwafor:** None. **K. Dennis:** Independent Contractor; Ontario Ministry of Health and Long-Term Care; Canadian Association of Radiation Oncology. **M.N. Reaume:** Honoraria; Merck, Novartis, Roche, Ipsen, Astra Zeneca, Eisai. Consultant; Pfizer, Astellas Pharma; Committee on Economic Analysis - Canadian Cancer Trials Group.

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Optimal timing of thoracic radiotherapy in limited stage small cell lung cancer (LS-SCLC) with daily fractionation: A national cancer database (NCDB) propensity matched analysis



R. White,¹ S. Hasan,² P. Renz,¹ S. Abel,³ Z. Otaibi,⁴ A. Colonias,³ D. Monga,⁵ and R.E. Wegner³;
¹Allegheny Health Network, Pittsburgh, PA, ²Allegheny Health Network Department of Radiation Oncology, Pittsburgh, PA, ³Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, ⁴Allegheny Health Network Division of Hematology/Oncology, Pittsburgh, PA, ⁵Allegheny Health Network Division of Medical Oncology, Pittsburgh, PA

Purpose/Objective(s): De Ruyscher et al. determined that survival in limited stage small cell lung cancer (LS-SCLC) improves the sooner thoracic radiotherapy (TRT) is initiated and completed following chemotherapy (CTX). However, that meta-analysis was largely based on twice daily treatment, which is only utilized approximately 10-15% of the time

in America. Therefore, we analyzed the national cancer database (NCDB) to determine the optimal treatment timing of TRT for LS-SCLC undergoing daily fractionation.

Materials/Methods: We queried the NCDB for LS-SCLC patients between the years 2004 – 2014 treated with doublet agent CTX and once-daily TRT in this IRB-exempt study. Chi square analysis determined clinical characteristics of patients more likely to start TRT within 30 days of CTX. Receiver operating characteristic (ROC) analysis determined optimal cutoff times for the initiation, duration, and completion of TRT following CTX with relation to survival. Multivariable cox regression analysis determined the association of such treatment timing parameters on survival.

Results: Ultimately 8990 patients treated to a median dose of 60 Gy (54 – 75 Gy) with once daily fractionation were eligible for analysis. Median survival for all patients was 20.7 months. TRT was initiated with the first cycle, 2nd cycle, or within 30 days of CTX in 25%, 50%, and 69% of cases, respectively. The median times for initiation, completion, and duration of TRT after CTX were 21, 70, and 50 days, respectively. Patients under 65, treated after 2007, treated to dose over 60 Gy, and with a lower T/N stage were all more likely to start TRT within 30 days of CTX. ROC analysis revealed the optimal cutoff times for initiation, completion, and duration of TRT following CTX were 29, 75, and 54 days, respectively. Propensity score-matched multivariable analysis revealed that initiation of TRT after 30 days of CTX (HR=1.07, P =0.015), completion of TRT after 75 days of CTX (HR=1.09, P=0.001), and elapsed days of TRT beyond 54 days (HR=1.18, P<0.001) were all associated with a 4.7%, 5.4%, and 6.3% reduced 3-year survival, respectively. Other predictors of reduced survival were male gender, higher income, higher T/N stage, and higher comorbidity score. As a continuous variable, days from CTX to initial TRT (HR=1.001), end of TRT (HR=1.002), and elapsed days of treatment (HR=1.007) were each independent predictors of survival as well (P <0.01).

Conclusion: Our NCDB-based study corroborates prior meta analyses that the sooner TRT is started and completed following CTX in LS-SCLC, even with daily fractionation, the better the outcome. Of all tested timing parameters, elapsed TRT time less than 55 days was the strongest predictor of survival.

Author Disclosure: R. White: None. S. Hasan: None. P. Renz: None. S. Abel: None. Z. Otaibi: None. A. Colonias: None. D. Monga: None. R.E. Wegner: None.

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Shorter Time To Treatment Initiation Does Not Improve Survival in Patients with Newly Diagnosed Small Cell Lung Cancer



A.G. Azzouqa, R. Manochakian, Y. Lou, and R. Chen; *Mayo Clinic Florida, Jacksonville, FL*

Purpose/Objective(s): Time to treatment initiation (TTI), after a new lung cancer diagnosis, is a controversial topic. Although it is considered an important aspect of healthcare quality, no clear evidence that links it to better clinical outcomes. Small Cell Lung Cancer (SCLC) is the most aggressive subtype of lung cancer and comprises about 13% of new lung cancer diagnoses in the USA. SCLC is characterized by rapid progression time, higher response rate to treatment and poor overall prognosis. These make a clinical argument that shorter TTI may lead to better clinical outcomes. The primary objective of this study is to determine if TTI is correlated with survival in patients with SCLC.

Materials/Methods: We reviewed data from our multi-site cancer center registry and identified all patients diagnosed with SCLC at our institution from 2000-2016. TTI was calculated from time of diagnosis to time of first treatment (Chemotherapy, radiation therapy or surgery). Analyses were performed by SAS software 9.4. Log-Rank test was used to compare survival. Cox regression multivariate model was used to evaluate the prognostic value of variables to survival.

Results: 1292 patients; 590 females (46%) and 702 males (54%) were reviewed. Median age at diagnosis was 68. 770 (60%) patients had

extensive stage and 494 (40%) had limited stage at diagnosis. Median TTI was 10 days. We compared outcomes of patients with TTI >10 days to TTI ≤10 days. Outcomes were stratified based on age, gender, and stage. Median Overall Survival (OS) for patients with TTI > 10 days was significantly better than patients with TTI ≤ 10 days (12.5 months vs. 9.1 months, P-value 0.0002). For patients with extensive stage, OS was better for TTI >10 days; 9.4 months vs. 7.4 months for patients with TTI ≤ 10 days, P-value 0.0006. For patients with limited stage, there was no statistically significant difference in OS among patients with TTI>10 days vs. patients with TTI ≤ 10 days (19.1 months vs. 16.0 months, P-value 0.7168). We also looked at different TTI thresholds, including 7 and 14 days and the findings were similar.

Conclusion: Shorter time to treatment initiation (TTI) in patients with newly diagnosed SCLC was associated with worse survival in patients with extensive stage, while no difference in survival was noted in patients with limited stage. This might be explained by the fact that symptomatic and higher burden disease patients, who have worse prognosis, were treated faster. Further studies, which could take into account extent of disease and clinical condition of patients may be helpful. Nevertheless, we still believe treatment for SCLC patients should be offered in a timely manner as it leads to shorter duration of emotional distress during the cancer management process.

Group	OS, TTI>cutoff	OS, TTI < cutoff	P-Value
>10or ≤10days	12.5 months	9.1 months	0.0002
>14or ≤14 days	13 months	9.4 months	0.0001
> 7or ≤ 7 days	11.8	9.4	0.031

Author Disclosure: A. Azzouqa: None. R. Manochakian: advisory board member; Takeda pharmaceutical company. Y. Lou: None. R. Chen: Employee; GlaxoSmithKline. Stock; Eli Lilly and Company, GlaxoSmithKline.

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Trends in IMRT Use for Limited Stage Small Cell Lung Cancer: A National Cancer Database Analysis



S. Hasan,¹ P. Renz,² A.T. Turrisi, III,³ A. Colonias,⁴ and R.E. Wegner⁴; ¹Allegheny Health Network Department of Radiation Oncology, Pittsburgh, PA, ²Allegheny Health Network, Pittsburgh, PA, ³James H Quillen VA Medical Center, Nashville, TN, ⁴Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA

Purpose/Objective(s): The standard of care for limited stage small cell lung cancer (SCLC) is concurrent chemoradiation, which can be delivered using 3D conformal radiation therapy (3D CRT) or intensity modulated radiation therapy (IMRT). We sought to use the National Cancer Database (NCDB) to identify predictors and trends in IMRT use for limited stage SCLC.

Materials/Methods: We queried the NCDB from 2004-2014 for limited stage SCLC patients that received chemotherapy and definitive doses of radiation to the chest using either 3D CRT or IMRT. Univariable and multivariable analyses were performed to identify sociodemographic, treatment, and tumor characteristics predictive of IMRT use and overall survival (OS). Propensity-adjusted Cox proportional hazard ratios for survival were used to account for indication bias.

Results: We found 9,970 patients treated as above, with 59% being treated with 3D CRT and 41% being treated with IMRT. The use of IMRT increased steadily between 2004 and 2014, starting at a rate of 11% and ending at 57%. Patients with higher education and treatment at an academic center were more likely to receive IMRT. Higher radiation dose and BID fractionation also were more likely to receive IMRT. IMRT use did not predict for OS. Predictors for OS on propensity-adjusted Cox analysis were BID treatment, younger age, female gender, and private insurance.

Conclusion: The use of IMRT in limited stage SCLC has steadily increased over the past 10-15 years. We expect these rates to continue to climb based on extrapolation from recommendations for non-small cell lung cancer (NSCLC).

Author Disclosure: S. Hasan: None. P. Renz: None. A.T. Turrisi: None. A. Colonias: None. R.E. Wegner: None.

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Retrospective Radiologic Evaluation of Lung Re-expansion after Radiation Therapy



E. Galvan and Y. Li; *UT Health San Antonio, Mays Cancer Center, San Antonio, TX*

Purpose/Objective(s): The goal of this project is to characterize rates of re-expansion of the collapsed lung after radiation therapy (RT) to the chest.

Materials/Methods: Retrospective analysis was performed at a single institution on 77 patients who underwent RT to the chest to malignancy causing collapse or significant post-obstructive atelectasis of one or more lobes of the lung, treated by single radiation oncologist specializing in lung cancer.

Results: Average follow-up was 6.8 months (median: 2.3 months) after RT. Nineteen (25%) patients died within 60 days of RT (10 died while on treatment), 12 (16%) enrolled in hospice within 60 days of finishing treatment. Sixty lesions were non-small-cell lung cancer (NSCLC), 11 were small-cell lung cancer (SCLC), 1 was likely thymus primary, and 5 were metastases from other sites. Patients were treated with palliative intent in 75% of cases. The average dose delivered was 3476cGy in 13 fractions. Pleural effusions were visualized pre-treatment in 45 patients (58%). Initial follow-up scans were available for 34 patients, performed an average of 32.5 days (median: 28; range: 0-154) after RT. Fifteen patients without pleural effusions had initial follow-up scans demonstrating improved aeration in 87% of these patients. Comparatively, nineteen patients with pleural effusion demonstrated aeration improvement in 63% of initial follow-up scans, with three patients' scans actually demonstrating worsening effusion or collapse. One patient with total lung collapse with partial improvement initially subsequently had re-collapse of the lung evident at 5-month follow-up. Follow-up scans at >2 months (average: 109 days, median: 92 days) were available for 22 patients; 16 patients had worsening effusion, worsening collapse, growing tumor, or no improvement at this time point; 3 had continued improvement from the initial post-treatment scan, and 3 had stable findings of re-aeration compared to the initial post-treatment scan.

Conclusion: Re-aeration, if it does occur, usually manifests at or before one-month post-RT for malignant pulmonary obstruction; meaningful re-aeration does not often occur after 2 months. The presence of a pleural effusion is a predictor of persistent collapse after RT to malignant lesions causing post-obstructive lobar collapse or atelectasis; effusion prevents the lung from re-expanding even after the bronchus becomes un-obstructed by tumor. If the goal of palliative thoracic RT is to improve dyspnea and functional respiratory capacity, then addressing the effusion with an additional intervention such as an indwelling tunneled catheter combined with aggressive pulmonary rehabilitation with intermittent positive pressure breathing (IPPB) using Continuous Positive Airway Pressure (CPAP) or BiLevel Positive Airway Pressure (Bi-PAP) devices may be considered to improve the rates of re-aeration.

Author Disclosure: E. Galvan: None. Y. Li: None.

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Digital Symptom Tracking, Patient Engagement and Quality of Life in Advanced Cancer



O. Generalova, E.T. Hall, B. Velazquez, and K.J. Ramchandran; *Stanford University, Palo Alto, CA*

Purpose/Objective(s): Patient reported outcomes (PROs) allow for systematic capturing of the patient experience. The recent evolution of PRO

instruments allows for routine tracking of the patient and family experience both between and at visits. PRO assessments have shown improvement in overall survival, enhanced patient physician communication, as well as improvement in quality of life and health care utilization. This study sought to explore the feasibility and impact of web-based PROs in advanced cancer patients, analyzing patient satisfaction, unplanned care, treatment adherence, and patient-provider communication. *Our hypothesis is that real-time, autonomous symptom tracking using a digital application is feasible at an academic medical center and will improve symptom management, improve patient quality of life, and decrease unplanned care.*

Materials/Methods: Our study is currently enrolling patients in several oncology disease groups at a single academic medical center. The participant population consists of individuals aged 18 years or older with a recurrent or metastatic advanced lung, gastrointestinal, renal, bladder or castrate resistant prostate cancer. Patients are randomized 1:1 to the intervention online PRO platform, or usual care. The Thoracic cohort has completed enrollment at 48 patients, with 74 patients enrolled in the study overall. In the PRO intervention group, patients complete symptom questionnaires prior to clinic visits and are prompted to complete weekly symptom diaries for the 6M study period. In both arms, patient reported health related quality of life (HRQL) is assessed at baseline, 3M, and 6M. Clinician (RN, MD, APP) and patient satisfaction is measured at the halfway point, as well as at study completion.

Results: We anticipate reporting the feasibility of the intervention, including patient satisfaction, adherence to scheduled symptom questionnaires, and clinician satisfaction within the Thoracic cohort. Additionally, we will document the difference in HRQL and unplanned health care usage between both groups.

Conclusion: Oncology patients are increasingly using PRO's to manage their symptoms, both in clinical trials and in normal practice. Our study assesses the feasibility and impact of an online symptom tracking tool on HRQL and unplanned medical care. We believe that PROs will be an integral component of high-quality cancer care and add to the literature that improves patient HRQL in advanced cancer patients.

Author Disclosure: O. Generalova: None. E.T. Hall: None. B. Velazquez: None. K.J. Ramchandran: None.

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Smoking History and Cessation Guidance in Lung Cancer Patients: A Review of Practice Patterns at Consultation



J.M. Holland,¹ E. Holland,² S. Brown,^{1,3} N. Desai,² K. Bernay,² C. Defrancesco,² and M. Wade²; ¹Oregon Health and Science University, Portland, OR, ²Oregon Health & Science University, Portland, OR, ³Oregon Health & Science University Department of Radiation Oncology, Portland, OR

Purpose/Objective(s): Smoking during lung cancer radiotherapy is associated with worse outcomes and increased toxicity. We evaluated tobacco use and tobacco cessation guidance in patients treated at an academic radiation oncology facility to improve practice.

Materials/Methods: Initial consultation notes of 174 consecutive non-metastatic lung cancer patients from January 2014 through June 2017 were reviewed using the electronic medical record. These notes contained input from residents, attendings and nurses. Descriptive statistics were used to evaluate tobacco use patterns, lung cancer histologies, staging and cessation guidelines.

Results: The most common lung cancer in this series was a PET-avid or growing lung nodule (35%) followed by adenocarcinoma (30%), squamous cell carcinoma (21%) and small cell (10%). Most patients had stage I disease (53%) followed by stage III disease (26%). Ninety-seven percent (168) were asked about smoking habits. The majority of patients were former smokers (60%) with 20% identified as quitting within the preceding year. Thirty-eight percent were current smokers. Only three patients (2%) in this series were identified as "never smokers". Current users smoked an average of 0.88 packs per day (range "few" to 4 packs per day). Current users reported an average of 55 pack years smoked (range 2 to 180 pack years). Of the sixty-three current smokers, discussions regarding cessation

were documented in only 35 patient encounters (56%). Twenty-four of these patients (69%) were identified as “ready to discuss cessation”. Nine of these patients (38%) received medical cessation therapy (6 nicotine patches, 3 nicotine gum/lozenges, and 1 varenicline.)

Conclusion:

1. The majority of lung cancer patients in our recent practice are former (60%) smokers.
2. Current smokers made up 38% of our population, which is slightly greater than twice the smoking rate of Oregon adults (17.7% in 2012).
3. In the era of stereotactic body radiotherapy (SBRT) for lung cancer, the greatest percentage of our patients represented PET-avid or growing lung nodules.
4. All patients need to be asked about smoking history and clinic staff need to be prepared to discuss cessation strategies.
5. The majority of current smokers in clinic are ready to discuss tobacco cessation.

Author Disclosure: J.M. Holland: None. E. Holland: None. S. Brown: None. N. Desai: None. K. Bernay: None. C. Defrancesco: None. M. Wade: None.

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The development and characterization of patient derived xenografts from non-small cell lung cancer brain metastases



A.M. Baschnagel, S. Kaushik, L.J. Abel, P. Clark, D. Buehler, and R.J. Kimple; *University of Wisconsin, Madison, WI*

Purpose/Objective(s): Brain metastases from non-small cell lung cancer (NSCLC) remain a significant challenge to treat and lead to the death of many patients. One of the major barriers to improving outcomes and developing novel treatments is the lack of preclinical models. We have developed a clinically relevant system to study NSCLC brain metastases, by establishing and characterizing a direct-from patient derived xenograft model of NSCLC brain metastases, including intracranial brain metastasis.

Materials/Methods: Patients diagnosed with NSCLC and brain metastases were consented for donation of brain tumor specimens. Surgically obtained tissue was implanted subcutaneously and as orthotopic intracranial implants into immunodeficient mice. Intracranial implanted tumors were monitored with a 4.7T MRI. During subsequent passages, formalin-fixed paraffin-embedded as well as flash-frozen tissues were harvested. Histology and immunoprofiles were compared between original tumor and subsequent xenograft passages. Tumors underwent RNA and DNA sequencing and relevant therapeutic targets were identified. Tumor growth rates and response to radiation, MEK inhibitor selumetinib and ATR inhibitor VX-970 were assessed and early passage cell strains were developed for rapid testing of drug sensitivity.

Results: Patient derived xenograft have been established in 7 of 12 patients to date. All seven xenografts are adenocarcinomas and have been passaged at least 5 times. The mean time from initial tumor implantation to first passage was 56.4 days and to second passage was 48.9 days ($P = 0.31$). Morphologically, strong retention of cytoarchitectural features was observed between original patient tumor and subcutaneous tumor xenografts. Intracranial tumor implants were successfully carried out and tumor histology and morphology was retained compared to original patient samples. Preservation of TTF-1 expression was seen in xenografts derived from NSCLCs originally positive for this marker. The most common genomic alteration was *KRAS* mutation, while all tumors were negative for *EGFR* and *ALK* alterations. Other relevant genomic alterations include *MYC* amplification and loss of *CDKN2A*. PD-L1 expression varied from <1% to 70%. RNA sequencing analysis demonstrated transcriptome concordance between patient tumor and the matched xenograft samples. Significant growth inhibition of representative xenografts was shown with radiation, selumetinib and VX-970 treatments delivered over one-two

weeks. Early passage cell strains showed high consistency in response to cancer therapy between xenograft and cell strain.

Conclusion: We have established a robust human xenograft model system for investigating NSCLC brain metastases. These patient derived xenografts show strong correlation with the original tumor specimens and provide a powerful resource for testing preclinical therapeutics.

Author Disclosure: A.M. Baschnagel: None. S. Kaushik: None. L.J. Abel: None. P. Clark: None. D. Buehler: None. R.J. Kimple: Employee; University of Wisconsin. Research Grant; Threshold Pharmaceuticals, Peloton Therapeutics, American Cancer Society, National Institute of Health, V Foundation for Cancer Research; International Journal of Radiation Oncology Biology Physics.

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Outcomes in Patients who have Undergone Multiple Lung SBRT Courses



J. Bloom,¹ G. Tolekidis,² P.A. Blumenfeld,² E. Ritz,² and G. Marwaha³; ¹Rush University Medical Center, Chicago, IL, ²Rush University Medical Center, Chicago, IL, ³Rush Medical Center, Chicago, IL

Purpose/Objective(s): The favorable local control rates and toxicity profile of lung stereotactic body radiation therapy (SBRT), in addition to patients living longer with oligometastatic disease, has led to SBRT's repeated use in patients with synchronous and metachronous lung nodules. While clinical symptoms from SBRT involving the central airway and chest wall, for example, have been described for single treatments, there is little data on multiple rounds of SBRT. Our purpose is to analyze a cohort of lung SBRT patients who have been treated with at least two courses of SBRT to assess for clinical outcomes and toxicities.

Materials/Methods: Thirty-four patients with 76 synchronous or metachronous lung nodules were treated with SBRT. Kaplan Meier survival analyses were employed to assess clinical outcomes. Toxicity was assessed using the standardized CTCAE 4.0 criteria.

Results: The median age of patients at their first SBRT was 72 years with a median ECOG score of 1. The most common dosing regimens were 54 Gy in three fractions (49.2%) and 50 Gy in five fractions (36.5%). Of the SBRT treatments, 55% were for primary tumors, 34% for oligometastatic disease, and 11% for salvage treatment. Median follow up time was 30.8 months. Twenty-seven (79.4%) patients received two SBRT courses; six (17.6%) underwent three SBRT courses; one (2.9%) underwent four SBRT courses. Of the 76 lesions treated, local control rate was 94.7% with overall survival of 70.6% (OS: primaries 60%, oligometastases 69%, salvages 100%) at 31 months. Distant metastasis occurred in 11 cases (14.5%). Fatigue, dyspnea and pneumonitis were the most common toxicities experienced. No toxicities above grade 2 were observed. Fatigue was present in 15 (44.1%) patients; this correlated with the number of courses of SBRT received ($p=0.04$). For example, 37% of patients who underwent 2 courses of SBRT experienced fatigue vs 67% who underwent 3 courses. Seven patients (20.6%) experienced grade 1 pneumonitis. These patients received a mean trachea/bronchial tree max dose of 29.02 vs 19.84 Gy in those with no pneumonitis ($p=0.13$). Eight patients (23.5%) experienced grade 1 or 2 dyspnea; these patients received a slightly higher trachea/bronchial tree max dose, 22.05 vs 21.63 Gy (NS). Five patients (14.7%) experienced grade 1 or 2 pain; these patients received a max dose to the chest wall of 61.69 vs 53.77 Gy (NS).

Conclusion: Recently, the use of repeat courses of SBRT for lung primaries and oligometastases in the same patient has increased. Our study showed similar favorable clinical outcomes of these treatments to those previously published: local control rate of 94.7% with overall survival of 70.6% at 31 months. Notably, not a single grade 3 toxicity occurred, suggesting multiple courses of SBRT is a safe and effective treatment regimen in this patient population.

Author Disclosure: J. Bloom: None. G. Tolekidis: None. P.A. Blumenfeld: None. E. Ritz: None. G. Marwaha: None.

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High Doses to the Heart Affect Overall Survival in Stage III Non-small Cell Lung Cancer Patients Undergoing Radiation Therapy



X. Liu,¹ S.E. Schild,² M. Fatyga,³ J.R. Niska,² M.G. Herman,⁴ and J. Li¹;
¹Arizona State University, Tempe, AZ, ²Department of Radiation Oncology, Mayo Clinic, Phoenix, AZ, ³Mayo Clinic Arizona, Phoenix, AZ, ⁴Mayo Clinic, Rochester, MN

Purpose/Objective(s): To determine if radiation induced cardiac toxicity influences overall survival (OS) in stage III non-small cell lung cancer patients undergoing radiation therapy (RT).

Materials/Methods: A single institution database of 134 stage III non-small cell lung cancer patients, treated with radiation therapy, was retrospectively analyzed in this study. Survival status for each patient was obtained from the institutional tumor registry. Patients were treated with conventionally fractionated 3D Conformal and Intensity Modulated Radiation Therapy. The heart structure was contoured for each patient within the treatment planning system. A range of dose volume histogram (DVH) indices was computed from the whole heart cumulative DVH and used together with patient specific characteristics in a family of Multivariate Cox Regression models. Each model used a single DVH index combined with prescription dose, age before RT, mean lung dose, lung V20, tumor location and laterality, disease stage, chemotherapy and surgery. The Akaike Information Criterion was used to find significant predictors in multivariate analysis. We used this method to search within a wide range of DVH indices for indices that may be predictive for a decrease in overall survival. Only one DVH index was used in each model because of strong correlations between indices derived from the same DVH. Subsequently, each heart was digitally subdivided into four parts along sup-inf and left-right axes. The same analysis was repeated using cumulative DVHs in each sub-part separately.

Results: 80 (60%) patients presented with stage IIIA and 54 (40%) with stage IIIB cancer. Doses prescribed were 61.9±6.8Gy in 2Gy fractions, and 113 (77%) patients also received chemotherapy. 53 (40%) patients were alive at the last follow-up, while 81 (60%) were not. High doses to the heart were found to be significant predictors for OS, specifically: V%_{55Gy} (p=0.01) and V%_{60Gy} (p=0.04). Three patient characteristics were also found to be predictive for OS in all models: cancer stage (IIIA/IIIB, p=0.02), chemotherapy (p<0.01) and age before RT (p=0.02). The analysis of digitally subdivided heart structures showed that V%_{55Gy} (p=0.01) and V%_{60Gy} (p=0.02) in the right-superior portion of the heart were significant predictors for the OS, while doses to the remaining three segments of the heart were not predictive. The index V%_D indicates the percentage of the volume receiving dose D or greater.

Conclusion: High doses to the heart in radiation therapy for stage III NSCLC patients were associated with a decrease in OS, especially high doses to the right-superior segment of the heart. Minimizing high doses to the superior-right segment of the heart may potentially improve OS for lung cancer patients and permit higher therapeutic doses.

Author Disclosure: X. Liu: None. S.E. Schild: Research Grant; Alliance. Honoraria; uptodate. Travel Expenses; Alliance; NCCN guideline panel on non-small cell lung cancer. Reviews NCI-sponsored cooperative lung cancer trials; NCI thoracic malignancy steering committee. M. Fatyga: None. J.R. Niska: None. M.G. Herman: None. J. Li: None.

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Dosimetric Association with Toxicity in Patients Undergoing Multiple Lung SBRT Courses



J. Bloom,¹ G. Tolekidis,² P.A. Blumenfeld,² E. Ritz,² and G. Marwaha³;
¹Rush University Medical Center, Chicago, IL, ²Rush University Medical Center, Chicago, IL, ³Department of Radiation Oncology, Rush University Medical Center, Chicago, IL

Purpose/Objective(s): Stereotactic body radiation therapy (SBRT) is an established standard of care for medically inoperable, early stage lung

cancers and is an increasingly utilized treatment strategy for oligometastases. Little data exists concerning the safety parameters of multiple lung SBRT courses and how toxicity guides consecutive treatment planning for a single patient's synchronous or metachronous lung tumors. Our goal is to assess dosimetric strength in relation to clinical toxicities to determine if patients undergoing multiple SBRT courses experience significant toxicities due to cumulative dosing.

Materials/Methods: 34 patients with 76 synchronous or metachronous lung nodules were treated with SBRT. Radiation was dosed in agreement with institutional single-treatment organ-based toxicity guidelines. Patients' dosimetric statistics were collected along with clinical toxicity correlates using CTCAE 4.0 criteria. T-tests were employed using SAS v9.4 to assess relationships between dosing and structures at risk.

Results: The median age of patients at first SBRT treatment was 72 years. Median follow-up time was 30.8 months. The most common dosing regimens were 54 Gy in 3 fractions (49.2%) and 50 Gy in 5 fractions (36.5%). Twenty-seven (79.4%) patients received 2 SBRT courses; 6 (17.6%)- 3 SBRT courses; 1 (2.9%)- 4 SBRT courses. Table 1 depicts the received dose of radiation for organs-at-risk.

Table 1 Cumulative Dosimetric Statistics (n=34)

Variable	Median (Gy)	Minimum (Gy)	Maximum (Gy)
Spinal Cord Dmax*	9.7	1.4	27.4
Esophagus Dmax*	10.2	1.8	42.5
Brachial Plexus Dmax*	0.3	0.1	24.1
Heart Dmax*	17.3	2.1	61.6
Great Vessels Dmax*	25.3	6.0	82.7
Trachea/bronchial tree Combined Dmax*	18.0	0.6	53.3
ChestWall Dmax*	57.4	23.5	108.8
Both Lungs minus ITV Mean Dose	5.3	2.5	12.6
Both Lungs minus ITV v20 Gy (in %)	5.9	1.9	23.7

* Dmax was measured at 0.03 cc Fatigue (44%) and dyspnea (24%) were the most common experienced toxicities. Fatigue correlated with the number of SBRT courses received (p=0.04). All association tests comparing organ-at-risk received dose and CTCAE clinical criteria were non-significant. The greatest association occurred between grade 1 pneumonitis and trachea/bronchial tree, Dmax 29.02 Gy in those with grade 1 vs 19.84 Gy in those with grade 0 (p=0.13). No toxicities above grade 2 were observed.

Conclusion: Our study showed no association between cumulative OAR doses and toxicities in patients treated with multiple SBRT courses. After careful consideration of prior dose, especially to defined critical structures, it seems multiple SBRT treatments to the thorax in select patients is safe and effective. Further research is necessary to understand safety parameters stratified by location and number of courses received.

Author Disclosure: J. Bloom: None. G. Tolekidis: None. P.A. Blumenfeld: None. E. Ritz: None. G. Marwaha: None.

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Cleaning up the dose spill in lung SBRT plans



G. Narayanasamy,¹ D. Desai,² E.P. Galhardo,¹ S. Morrill,¹ J.A. Penagaricano,¹ and S. Maraboyina¹;
¹University of Arkansas for Medical Sciences, Little Rock, AR, ²Memorial Hospital, Chattanooga, TN

Purpose/Objective(s): We investigated 2 planning techniques that can reduce R50% and D2cm values in lung SBRT plans. These techniques include a) introduction of non-coplanar beams and b) reduction of mean dose to a 5 mm wide rind outside the PTV.

Materials/Methods: Dose fall-off was studied in 146 lung SBRT plans of patients treated between 2012 and 2017. Evaluated values of R50%, D2cm were compared against the maximum values specified in RTOG report # 0915. Deviations in R50% and D2cm were correlated with six plan

parameters including prescription dose, tumor location, number of beams or arcs, beam configuration (coplanar or non-coplanar), type of treatment plan (IMRT or VMAT), and shortest distance to the chest wall. A chi-square or Mann-Whitney correlation statistic was performed on R50% and D2cm against the aforementioned parameters. During this investigation, seven of eight plans with R50% deviations and 10 of 13 with D2cm deviations were found to be coplanar, establishing that coplanar techniques could result in larger dose spillage than non-coplanar techniques. For non-coplanar planning techniques, VMAT plans with deviations in R50% and/or D2cm were re-planned by revising the couch angle to ± 10 degrees and were re-evaluated for clinical acceptability based on the RTOG metrics. After the evaluation, higher mean dose to the first 5 mm rind outside PTV was observed on cases with high R50%. Therefore, a second planning technique of re-optimization was performed by inclusion of mean dose to the first 5 mm rind outside the PTV.

Results: All plans met the dose conformity index, target coverage, homogeneity index, and critical organ dose tolerance objectives. Significantly large number of deviations are seen in either R50% or D2cm in coplanar plans than non-coplanar plans (p -value <0.001). The deviation does not depend on any of the other mentioned parameters with p -values > 0.05 . Re-planning with a ± 100 couch angle was performed, and all VMAT plans showed a decrease in R50% and D2cm and eight out of 12 VMAT plans successfully met the RTOG-0915 criteria. The other four had a lower R50% in the range of 0.0–0.7 and D2cm lowered by 0.3%–8.5%, relative to the original plan. In the second planning technique involving re-optimization using mean dose to the first 5 mm rind, 5 VMAT plans having higher than acceptable R50% values were re-optimized resulting in R50% reduction by $2.7 \pm 0.6\%$.

Conclusion: This study shows that introduction of non-coplanarity plans and/or adding the optimization constraint to the mean dose to a 5 mm rind outside the PTV can lead to reduction in the dose spillage in lung SBRT plans.

Author Disclosure: G. Narayanasamy: None. D. Desai: None. E.P. Galhardo: None. S. Morrill: None. J.A. Penagaricano: None. S. Maraboyina: None.

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MR-Guided SBRT Boost for Locally Advanced NSCLC: Feasibility Study to Improve Local Control and Decrease Toxicity



A. Burr,¹ J.S. Witt,¹ K. Mittauer,¹ T. Christianson,¹ B.A. Perez,² T.J. Dilling,² A.M. Baschnagel,¹ M.F. Bassetti,¹ and S.A. Rosenberg²;
¹Department of Human Oncology, University of Wisconsin Hospital and Clinics, Madison, WI, ²H. Lee Moffitt Cancer Center and Research Institute, Department of Radiation Oncology, Tampa, FL

Purpose/Objective(s): Results from randomized dose escalation studies for locally advanced non-small cell lung cancer (NSCLC) have been disappointing. Secondary analysis of RTOG 0617 indicates that dose escalation may have failed because of increased cardiopulmonary toxicity. MR-guided treatment delivery allows for real time visualization of targets and the use of small margins for treatment. We hypothesized that using an MR-guided (MRIdian system) approach to deliver a conventionally fractionated plan with an SBRT boost would significantly decrease target volume size and allow significantly lower dose to organs at risk (OAR).

Materials/Methods: Six patients with locally advanced NSCLC were included in our dosimetric analysis. Patients were re-planned to 60 Gy in 30 fractions followed by a 20 Gy in 5 fraction boost (BED 102, alpha/beta

10) using ITV (internal target volume), MR-guided, or RPM-gated (real-time position) approaches. A breath hold for both MR-guided and RPM gated was simulated by contouring on the maximum inspiration phase of the 4D CT. The CTV to PTV expansions with RPM gating were 5.7 mm (L/R), 5.6 mm (A/P), and 6.3 mm (S/I), derived from institutional averages. Volume expansions are summarized in Table 1 and reflect uncertainty of set up with each motion management modality:

Dose constraints from RTOG 0617 were utilized as well as a more aggressive heart constraints (ex: heart mean < 20 Gy). These constraints were converted into BED equivalents for treatment planning given the different dose/fraction schedules.

Results: Five of the six patients planned with MR-guided treatment were able to meet constraints. The patient unable to meet constraints had a PTV of 533 cm³. The mean GTV and PTV of those patients successfully planned with MR-guided were 37.4 cm³ (range 6.4-81.6) and 139.7 cm³ (range 65.1-231.8), respectively. For MR-guided treatment, the mean lung dose was 11.5 Gy (range 6.4-17.4), heart dose 7.3 Gy (range 1.7-16.5), and V20=20.1% (range 9.7-32.9%). Coverage was excellent for all five MR-guided plans with 99% of the PTV receiving $>95\%$ of the dose. MR-guided planning reduced the PTV60 volume on average 36% and 31% compared to an ITV and RPM-gated plans, respectively. Our presentation will include dosimetric comparison to organs at risk with each motion management system.

Conclusion: These early results suggest that treatment planning with MRIdian system offers a possible method of dose escalation while decreasing toxicity. This lays the ground work for a potential MR-guided trial with advanced NSCLC to improve local control while sparing OAR with real-time visualization.

Author Disclosure: A. Burr: None. J.S. Witt: None. K. Mittauer: Honoraria; Viewray. T. Christianson: None. B.A. Perez: Advisory Board; BMS. T.J. Dilling: NCCN. A.M. Baschnagel: None. M.F. Bassetti: Stock; Seattle genetics. S.A. Rosenberg: None.

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Lung Stereotactic Ablative Radiotherapy (SABR) Following Pneumonectomy: A Systematic Review of Clinical and Toxicity Outcomes



A.J. Arifin,¹ F. Al-Shafa,¹ G. Boldt,¹ A. Warner,¹ G. Rodrigues,¹ D.A. Palma,¹ and A.V. Louie²;
¹London Regional Cancer Program, London, ON, Canada, ²Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Purpose/Objective(s): Survivors of lung cancer are at risk of second primary lung cancers (SPLCs), which are often curable. However, in patients who have previously undergone pneumonectomy, treatments options are limited. The aim of this study is to perform a systematic review of publications examining treatment planning considerations, clinical outcomes, and toxicity rates of SABR following pneumonectomy.

Materials/Methods: A systematic review of the literature was conducted in accordance with PRISMA guidelines using PubMed and EMBASE from inception to July 2018. A total of 220 entries were identified. Articles were limited to those published in the English language. 114 unique articles were assessed for eligibility. Inclusion criteria consisted of non-review articles with at least two patients who received exclusively lung SABR post-pneumonectomy. Two reviewers independently performed abstract and full-text review, with discrepancies settled by a third reviewer.

Results: Of the 114 articles identified by the initial search, five articles comprising 51 patients who received lung SABR post-pneumonectomy

Table 1 Different volume expansions based on different motion management systems

ITV-Based	ITV + 5mm = CTV60	CTV60 + 5mm = PTV60	Boost (PTV20) = ITV + 5mm
RPM-Gated	GTV + 5mm = CTV60	CTV60 + 5.6-6.3mm = PTV60	Boost (PTV20) = GTV + 5.6-6.3 mm
MR-Guided	GTV + 5mm = CTV60	CTV60 + 3mm = PTV60	Boost (PTV20) = GTV + 3mm

met inclusion criteria. Median age was 69 (range 69-74), and most patients were male (median 77.8%, 76.9-100%, n=3). The weighted average incidence of grade 3 or higher toxicity was 13.6% (0-33.3%, n=5). There was one treatment-related death from one case report that was infectious in nature, but the attributable effects of radiation could not be ruled out. The median 1-year rate of logoregional control was 90.5% (range 84.0-100%, n=4), which is consistent with previously published SABR data. Median BED10 was 105.6 Gy (87.5-151 Gy, n=5), and the most common dose fractionation schemes were 54 Gy in 3 fractions (n=3), 48 Gy in 4 fractions (n=3), and 60 Gy in 3 fractions (n=2). All of the studies used 4DCT image acquisition, a technique that captures a 3DCT volume over a period of time thereby describing the motion of a desired target. Respiratory gating was only employed in a single study.

Conclusion: SABR appears to be a safe and effective option for solitary pulmonary nodules in survivors of lung cancer with prior pneumonectomy. Multi-institutional and/or prospective studies would be helpful to determine the true risk and appropriateness of SABR in this high-risk patient population.

Author Disclosure: **A.J. Arifin:** None. **F. Al-Shafa:** None. **G. Boldt:** None. **A. Warner:** None. **G. Rodrigues:** Independent Contractor; George Rodrigues Medicine Professional Corporation. Stock; George Rodrigues Medicine Professional Corporation. Royalty; Demos Medical Publishing. **D.A. Palma:** Research Grant; Ontario Institute for Cancer Research. Patent/License Fees/Copyright; U.S. Patent Pending. **A.V. Louie:** Honoraria; Varian Medical Systems Inc.

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Inoperable Pulmonary Carcinoid Tumors: Local control rates with stereotactic body radiotherapy



D.P. Singh,^{1,2} M.A. Cummings,³ Y. Chen,⁴ and M.T. Milano²; ¹Wilmot Cancer Institute, University of Rochester, Rochester, NY, ²Department of

Radiation Oncology, University of Rochester Medical Center, Rochester, NY, ³University of Rochester Medical Center, Rochester, NY, ⁴Wilmot Cancer Institute, University of Rochester, Rochester, NY

Purpose/Objective(s): Surgery is the standard of care for pulmonary carcinoid tumors; however, options for inoperable patients are few. This study reports the outcomes of inoperable pulmonary carcinoid patients treated with stereotactic radiation therapy (SBRT).

Materials/Methods: From an institutional database, we retrospectively identified patients treated with SBRT for pulmonary carcinoid tumors 2007-2017. Additional inclusion criteria were prior histopathologic diagnosis, age > 18 years and KPS ≥ 70. Medical records were reviewed for patient characteristics, treatment details and outcomes.

Results: Ten patients were treated for 12 pulmonary carcinoid lesions with 5-10 fractions of SBRT between 2007-2017. Their median age was 66.5 years (range 40-83) and most presented with non-specific symptoms of cough, shortness of breath or hemoptysis. Pathology revealed typical carcinoid for 9 patients, with the tenth displaying atypical histology. Carcinoid tumor was located centrally in six patients, and peripherally in 4. The median prescription dose for all patients was 50 Gy in 5-10 fractions (range 40-60 Gy) with SBRT delivered using a stereotactic x-ray positioning system. Four patients received 10-fraction SBRT and 6 others received 5-fraction SBRT. The follow-up after SBRT ranged from 6-56 months, with a median of 25 months. Four patients were alive with stable disease at their last follow-up; two died from progression of disease and 4 died from other co-morbidities. Median overall survival was 27.1 months (range 5.5 months to 56 months).

Conclusion: Pulmonary carcinoid tumors treated with SBRT have promising tumor control rate and survival.

Author Disclosure: **D.P. Singh:** None. **M.A. Cummings:** None. **Y. Chen:** None. **M.T. Milano:** Honoraria; UpToDate.

Table 1

Patient #	Age / Sex	Presenting Symptoms	Typical / Atypical Carcinoid	Ki-67 (%)	Lesion # = Size (mm)	Peripheral / Central	Dose (Gy) / Fractions	BED (Gy)	EQD2 (Gy)	Local control	Disease status	Alive / Dead	Survival (months)	RT-Related Complications
1	77/F	C/SOB	TC	5	1 = <10 2 = 11-20	Central	50/5	100	83.3	Yes	Stable	Dead	34	None
2	51/F	C/SOB	TC	NR	1 = 11-20	Peripheral	50/5	100	83.3	Yes	Stable	Dead	56	None
3	66/F	C/SOB	TC	1	1 = 41-50	Central	50/5	100	83.3	Yes	Stable	Alive	16	None
4	57/F	Hemoptysis	TC	2	1 = 11-20	Peripheral	55/5	115.5	96.5	Yes	Stable	Alive	30	Focal Fibrosis
5	67/M	C/SOB	AC	NR	1 = 21-30	Central	50/10	75*	62.5	Yes	POD	Alive	36	None
6	58/M	Incidental	TC	2	1 = 31-40	Central	60/10	96	80.0	Yes	Stable	Dead	51	None
7	74/M	C/SOB	TC	2	1 = >50	Peripheral	55/11	82.5	68.8	Yes	POD	Dead	20	None
8	83/M	Hemoptysis	TC	2	1 = 31-40	Central	50/10	75	62.5	Yes	Stable	Dead	18	None
9	81/M	Incidental	TC	10	1 = <10 2 = <10	Peripheral	50/5	100	83.3	Yes	POD	Dead	6	Pneumonitis Grade III
10	40/F	C/SOB	TC	NR	1 = 11-20	Central	50/5	100	83.3	Yes	Stable	Alive	16	None

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