Materials/Methods: Enrollment goals are 244 subjects at up to 10 cancer centers worldwide. Eligibility criteria include stage IIIA-IIIC (AJCC v8) NSCLC; baseline grade 0-2 dyspnea, cough, and dysphagia; and no contralateral hilar or supraclavicular/cervical lymph node involvement. Subjects will be randomized (1:1) to CBCT-based daily ART or non-adapted RT using IMRT or VMAT delivering 60-66 Gy in 30-33 fractions with concurrent platinum doublet chemotherapy. Adjuvant immunotherapy with durvalumab is permitted. Follow-up for study participants will be for 1-year post-completion of chemoRT. Study endpoints include: frequency of PRO-CTCAE score ≥3 cough, dyspnea, or dysphagia from randomization to 30 days post-chemoRT; patient-reported quality of life (FACT-L and EQ-5D-5L questionnaires); percentage of lung receiving ≥20 Gy; mean doses to lung, heart, and esophagus; primary tumor response on CT or PET-CT (RECIST v1.1); local disease progression; and incidence of grade ≥2 pneumonitis within 1 year. Stratification factors are the treating institution and the presence of contralateral mediastinal lymph node metastases (associated with increased volume of irradiated lung). Interim analyses for futility and superiority will be performed when the primary endpoint data have been collected for 50% of evaluable participants.

Results: This study opened to enrollment on 20 October 2022 and is expected to be completed in approximately 3 years.

Conclusion: This prospective, randomized clinical trial rigorously evaluates the impacts of daily online ART on radiation pneumonitis, esophagitis, and quality of life in patients with advanced NSCLC. It will collect standard tumor response and disease progression metrics to assure that reduced margins do not have an adverse impact on outcomes. Online ART is emerging as an innovative approach enabling increased sparing of normal tissues. The results of this clinical study will support evidence-based clinical decisions around ART technologies.

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Radiation-Induced Brachial Plexopathy (RIBP) after Stereotactic Body Radiotherapy (SBRT): Pooled Analyses of Risks

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Purpose/Objective(s): RIBP, with symptomatic upper extremity motor or sensory deficits, is a risk after SBRT. We herein model dosimetric factors associated with risks of RIBP of the inferior aspect of the brachial plexus following SBRT for apical lung tumors.

Materials/Methods: Literature searches (PubMed & Embase databases) were performed to identify reports published from 2000-2021, using search criteria of ["brachial plex*" and stereotactic]. From a PRISMA systematic review, studies were identified that included individual patient data on: (1) RIBP endpoints after SBRT for apical lung tumors; and (2) brachial plexus Dmax, or maximum point doses (i.e., D0.035cc or D0.03cc). These data were amenable to normal tissue complication probability (NTCP) modelling. Doses were converted using the linear-quadratic model with an alpha-beta ratio of 3 Gy. For the probit models, the parameter values were determined using the maximum likelihood method and the 95% confidence intervals (CI) were determined using the profile likelihood method. The ability of the NTCP models to distinguish patients with and without RIBP was evaluated using the area under the curve (AUC).

Results: Two probit NTCP models were derived: one from 3 studies (185 patients with 192 targets and 11 events) and another from 4 studies (221 patients with 229 targets and 18 events). NTCP models (summarized in table) suggest ≈10% risks associated with brachial plexus maximum dose (Dmax) of ~32-34 Gy in 3 fractions and ~40-43 Gy in 5 fractions, with a clear dose response. These dose-responses with SBRT (with steep dose gradients beyond the target volume and thus only partial-irradiation of the brachial plexus) are far less steep than those reported following conventionally-fractionated or moderately-hypofractionated radiotherapy used for breast, lung and head and neck cancers (that tend to use radiotherapy fields that circumferentially irradiate the brachial plexus).

Conclusion: A dose-response for risk of RIBP after SBRT is observed relative to brachial plexus Dmax. The less-steep dose-response compared to that seen from conventionally-fractionated or moderately-hypofractionated radiotherapy (with large irradiated plexus volumes) suggest a possible volume dependence of RIBP risks. Future work should focus on understanding possible volume effects.

Abstract 2091 — Table 1

Patient cohort	*Predicted risk*	*AUC*	*OR (95% CI)*	*Dose threshold**	*p-value*
3 fraction equivalents					
4 studies	8.0%	0.78	14.3 (4.1-49.2)	55 Gy	<0.01
3 studies	5.9%	0.76	16.2 (3.1-85.0)	55 Gy	<0.01
5 fraction equivalents					
4 studies	8.0%	0.78	14.3 (4.1-49.2)	70 Gy	<0.01
3 studies	5.9%	0.76	16.2 (3.1-85.0)	70 Gy	<0.01
2 Gy / fraction equivalent					
4 studies	8.0%	0.77	13.6 (2.5-73.3)	355 Gy	<0.01
3 studies	5.9%	0.70	16.2 (3.1-85.0)	230 Gy	<0.01

* Beyond which the complication risk increases by corresponding OR

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Assessing Patterns of Practice in Early-Stage Lung Cancer Radiation Therapy: Findings from a Large Statewide Consortium Study on Hypofractionation

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Purpose/Objective(s): There are many different acceptable radiation dose and fractionation regimens for the treatment of early-stage non-small cell lung cancer (NSCLC), including hypofractionation (HypoRT). There are limited data supporting when to use HypoRT. We investigated which factors led physicians to choose HypoRT rather than stereotactic body radiation therapy (SBRT) or conventional fractionation (CRT) for early-stage NSCLC patients in a statewide consortium.

Materials/Methods: We examined patients with T1-3N0M0 NSCLC treated at multiple institutions in a statewide consortium from January 2012-July 2022. We classified treatments as SBRT if 5 fractions or fewer, HypoRT if 6-20 fractions, and CRT if 1.8-2 Gy per fraction (Gy/Fx) for 25 or greater fractions. We excluded patients between 20 and 25 fractions as most appeared to be CRT that did not finish treatment (5% of total). We then performed a classification tree using age, race, gender, smoking status, T stage, PTV within 2cm of esophagus, PTV within 2cm of heart, and concurrent chemotherapy as covariates with a three-variable output (SBRT, HypoRT, and CRT). We excluded ECOG as it was not significant on initial analysis and was missing for 100 patients. We also reran the classification tree without CRT as an output to better discriminate between SBRT and HypoRT.

Results: A total of 418 patients were included in the analysis. 184 patients had T1, 123 with T2, and 111 with T3 tumors. In total, 228 patients underwent SBRT (median 50 Gy), 51 patients HypoRT (median 60 Gy), and 139 CRT (median 63 Gy). Covariates significant for discriminating between all three treatment regimens included T2, T3 vs T1, PTV within 2cm of the esophagus, and T3 vs T2. 94% of T1 patients were treated with SBRT. Among T2 and T3 patients, those within 2cm of the esophagus were significantly more likely to be treated with CRT or HypoRT (80% vs 15%). Patients with T3 tumor not within 2cm of the esophagus, were more likely to be treated with CRT or HypoRT than the T2 patients (85% vs 36%). Patients treated with CRT were also more likely to receive chemotherapy, particularly for T3 tumors (80% received concurrent chemotherapy). Excluding CRT as an output variable, proximity to the heart became significant in addition to the other previously described covariates. Notably, the branch with the highest likelihood of HypoRT were patients with T2/T3 tumors within 2 cm of both the esophagus and heart (94% HypoRT vs 6% SBRT). Patients with tumors not close to central structures but with T3 rather than T2 tumors were more likely to be treated with HypoRT as well (62% vs 38%).

Conclusion: Based on this large prospective real-world data of early-stage NSCLC, larger tumors and those located near central structures are more likely to be treated with HypoRT. The patient's age, performance status, race, and smoking status were not significant in this analysis. Additional analysis on outcomes and toxicity related to treatments is underway.

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Predictive Factors for Response to Adaptive Therapy in Thoracic Stereotactic Ablative Radiotherapy

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Purpose/Objective(s): Online adaptive radiotherapy (ART) has been increasingly adopted for clinical use. However, ART for thoracic malignancies has lagged beyond its implementation for other primary cancers. Efforts are needed to identify optimal patients for ART by finding trends for changes in tumor position, shape, or proximity to OARs are needed. We hypothesized tumor size, histology, pre-RT SUV value, and intrathoracic location could influence how tumors change during cone beam computed tomography (CBCT)-based ART Stereotactic Ablative Radiotherapy (SAbR) for thoracic disease.

Materials/Methods: Data was collected from a prospective registry of patients who received CBCT-ART and SAbR for primary and secondary lung tumors. Dosimetry data was obtained from the simulation planning and the daily adaptive workflow. Central lung tumors were defined as those located within 2 cm of the bronchial tree. Plans were either delivered as per simulation or through the online adaptive workflow delivery (AD). Change in planning tumor volumes (PTV) were calculated between initial and final fractions (ΔPTV).

Results: A total of 42 patients with a median age of 67 (range 17-90) and median 8.3 months follow up, treated between June 2021 and December 2022 were included. Most patients had NSCLC or presumed NSCLC (73.85%, 31/42), and most lesions were peripheral (61.9%, 26/42) versus central (31%, 13/42) or apical (7.1%, 3/42). Mean dose and median fractions were 52.5 Gy (SD 8.07) and 5 (range 3-5) while median initial (i) PTV was 31.75 cm^3 (IQR 42.3 cm^3). On average, ΔPTV decreased by 4.9% (SD 21) and volume shrunk by 5 cm^3 (SD 14.5). AD improved per fraction PTV coverage and conformality while esophageal, cardiac, and spinal cord dose were significantly decreased (all $p < 0.05$), and most fractions were delivered with AD (73.4%, 138/188). AD was aborted most often for small iPTVs. ΔPTV grew >10% for two lesions though their iPTV were < 10 cm^3. 12/42 ΔPTV were >10% smaller by the end of RT and corresponded to larger iPTVs. Age, lung primary, metastatic disease, smoking status, and tumor location were not predictive for >10% decrease in ΔPTV. Among 24 biopsy-proven NSCLC ΔPTV was >10% smaller in 6/12 patients (50%) with adenocarcinoma and only in 2/12 (16.7%) with SCC, although this was not significant on χ^2 testing ($p = 0.08$). There were no differences in local, regional, distant failure or death comparing those with a ΔPTV of >10% vs <10% (all $p > 0.1$). Comparing pre-treatment PET SUV and tumor response, lower SUVs appear to be associated with more PTV shrinkage, with no significant PTV change plateauing at SUV 20. However, this analysis was limited by the number of patients with high SUV values.

Conclusion: CBCT-ART SAbR is associated with improved PTV coverage, target conformality, and reduced OAR dose. Large iPTV and adenocarcinomas were more likely to decrease >10%. High metabolic activity appeared predictive for a lack of significant ΔPTV. Further clinical and radiographic features should be explored to predict response to ART.

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A U.S. Cancer Center's Interactive Cancer Education Program for Spanish-Speaking Latinos during COVID-19 Pandemic

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Purpose/Objective(s): Cancer is a leading cause of mortality in U.S. Latino adults, a group with limited access to screening, higher rates of advanced disease, and prone to online misinformation. Our project created a Facebook Live social media video campaign on general cancer prevention, screening, risk, information, and resources, targeting Spanish-monolingual Latinos during the COVID-19 pandemic.

Materials/Methods: Our project consisted of a hybrid video campaign model released to Facebook social media platform between October and December 2021, where pre-recorded videos or livestream interviews were delivered in Spanish with auto-generated, language-concordant subtitles to increase accessibility for the hearing-impaired. The videos featured fluent and ethnically concordant cancer topic experts. The content of these videos