

# Clinical and Dosimetric Factors Impacting Radiation Pneumonitis in Isotoxically Dose-Escalated NSCLC

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## Purpose/Objective(s)

Radiation pneumonitis (RP) has been related to various clinical and radiation dosimetric factors such as mean lung equivalent dose in 2 Gy fractions (ML-EQD2). Here we test the hypothesis that other factors impact grade 2 or higher RP within 6 months of radiotherapy (RT) ( $\geq$ G2RP) when ML-EQD2 is controlled via isotoxic dose-escalation.

## Materials/Methods

We analyzed 114 patients treated to doses of 63-73 Gy in 30 fractions over 5 or 6 weeks in a prospective trial of isotoxically escalated RT with concurrent chemotherapy (CT). The predicted rate of  $\geq$ G2RP was 20%. An initial prescribed tumor dose (PD) was selected to achieve ML-EQD2 of 18.2 Gy. PD was reduced by 10% for CT toxicity, and further to meet other organ constraints. Dose volume histograms (DVHs) were extracted for these structures: Whole lung minus GTV (L-GTV), lung on contralateral (CL) and ipsilateral (IL) sides of the tumor, CL and IL split into equal thirds (upper, middle, and lower sections). Ninety-five percent of the variance between L-GTV DVHs was represented by 7 principal components (PC) with eigenvalue  $>1$ . Maximum RP scores within 6 months of RT were collated. Univariable logistic regression analysis (UVA) was performed to ascertain associations of clinical factors, L-GTV PCs and ML-EQD2 with  $\geq$ G2RP risk. Model 1 represents the best multivariable (MV) model obtained from these factors via stepwise selection using Akaike information criterion. The significant L-GTV PC in the MV model was replaced by the L-GTV and CL/IL section volumes irradiated to the dose levels represented by that PC for further localization.

## Results

Mean PD was 67.1 Gy. ML-EQD2 mean was 14.4 Gy (95% CI = 13.9-14.9). The  $\geq$ G2RP rate was 26%. On UVA, there was no evidence that ML-EQD2 mean was associated with  $\geq$ G2RP risk, but  $\geq$ G2RP risk increased with poor PS and high L-GTV PC5 (representing greater L-GTV volumes receiving 6-9 Gy, L-GTV<sub>6-9</sub>). L-GTV PC5, poor PS, and high baseline FVC (FVC0) were significantly associated with  $\geq$ G2RP

risk (MV Model 1). L-GTV<sub>6-9</sub> and CL lower segment (CLL) receiving 6-9 Gy (CLL<sub>6-9</sub>) were significantly associated with ≥G2RP risk when they replace L-GTV PC5 (MV model 2 and 3).

## Conclusion

ML-EQD2 mean is a poor predictor for ≥G2RP in these isotoxically escalated patients, amongst whom there was limited lung mean dose variability. Poor PS, high FVC0 and greater lung volumes receiving 6-9 Gy were associated with increased ≥G2RP risk.

Abstract 329; Table 1.

Variables	UVA	MVA		
	OR (95% CI) <i>P</i> -value	1 OR (95% CI) <i>P</i> -value	2 OR (95% CI) <i>P</i> -value	3 OR (95% CI) <i>P</i> -value
PS 1 Vs 0	2.447 (1.005-5.961) 0.049	3.716 (1.370 - 10.084) .010	3.433 (1.298 - 9.078) .013	3.484 (1.316 - 9.224) .012
PD	1.064 (0.946-1.197) 0.298	-	-	-
PTV	1.001 (0.999-1.003) 0.511	-	-	-
ML-EQD2mean	0.961 (0.823-1.123) 0.617	-	-	-
FVC0	1.018 (0.885-1.042) 0.115	1.025 (1.000 -1.050) .049	1.026 (1.001 - 1.051) .038	1.023 ( .998 - 1.048) .067
L-GTV PC5	1.578 (1.050 - 2.373) .028	1.738 (1.138 - 2.654) .010	N/C	N/C
L-GTV <sub>6-9</sub>	1.089 ( .999 - 1.188) .053	N/C	1.114 (1.014 - 1.223) .025	N/C
CLL <sub>6-9</sub>	1.053 (1.001 - 1.107) .048	N/C	N/C	1.060 (1.004 - 1.119) .036

N/C = not considered

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