Purpose: The relationship between spatial aspects of the dose distribution and incidence of acute radiation esophagitis for non-small-cell lung cancer (NSCLC) patients is not well understood. Specifically, the location of dose along the superior-inferior (SI) axis of the esophagus has not been previously considered. We introduce the concept of mean regional dose (MRD) calculated for esophageal subvolumes, and test for significance for prediction of acute esophagitis (AE).

Methods: The 3D dose distribution within the esophagus was extracted for 541 NSCLC patients treated with definitive photon therapy. The esophagus contour was divided into equal geometric halves, thirds, and fourths along the SI direction of the structure. MRD in each subvolume was calculated. Univariate logistic regression was performed to determine the correlation between MRD and CTCAE3.0 AE grade ≥ 2 (medical intervention). The MRD was incorporated into an existing NTCP model (based on mean dose for the total esophageal volume) as a separate additive factor.

Results: Univariate analysis indicated a significant correlation between AE grade ≥ 2 and MRD in each of the esophageal subvolumes except for the inferior third and inferior-most quarter. There was a statistically significant improvement when including the additive MRD factor for the superior/inferior halves, superior/inferior thirds, and superior-most/inferior-most quarters into the NTCP model.

Conclusions: This study investigates previously unexplored regional differences in delivered dose to the esophagus of patients treated for NSCLC. There is evidence to suggest that dose to the superior portions of the esophagus is more important as it relates to the potential for acute toxicity. The 541 patient cohort is the largest database used to investigate AE in patients treated for NSCLC, strengthening the power of the statistical results. Additional methods to incorporate dose in individual esophagus voxels (along the SI axis) into the NTCP model are also being explored.