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## Substantial Dose-response Relationship with Clinical Outcome for Lung Stereotactic Body Radiotherapy (SBRT) Delivered via Online Image Guidance

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## Purpose

To examine potential tumor dose-response relationships with various non-small cell lung cancer (NSCLC) SBRT fractionation regimens delivered with online CT-based image guidance.

## Materials/Methods

Four-hundred-four (404) tumors in 382 patients with clinical stage T1-T2 N0 NSCLC were treated with CT-based (Elekta cone-beam CT) online image-guided SBRT at 5 institutions (1998-2009) and had available 3D dose-volume data for the gross tumor volume (GTV) and planning target volume (PTV). All cases were planned with heterogeneity correction. Median maximum tumor dimension was 2.4 cm (range 0.9-7.3 cm). Dose fractionation prescription was according to each institution's protocol with the most common schedules of 18-20 Gy x 3, 12 Gy x 4, 12 Gy x 5, 12.5 Gy x 3, 7.5 Gy x 8 (median=54 Gy, 3 fractions). Median prescription (Rx) BED<sub>10</sub>=132 Gy (60-180). Median values (Gy) of 3D planned doses for BED<sub>10</sub> were GTVmin=165, GTVmean=190, GTVmax=207, PTVmin=115, PTV D99=116, PTVmean=166, PTV D1=199, PTVmax=207. Mean follow-up=1.3 years.

## Results

Twenty-two (22) cases (5%) had local recurrence (LR) for a 2-year rate of 9%. All BED<sub>10</sub> GTV & PTV endpoints were significantly associated with LR (p<0.01) as continuous variables on univariate analysis. PTV mean dose appeared to have the highest correlation with LR with area under ROC curve of 0.74 (p<0.01) and an optimal cut point of 125 Gy BED<sub>10</sub>. Two-year LR was 4% for PTVmean >125 vs 30% for < 125 Gy (p<0.01) with sensitivity=87% and specificity=59% for predicting LR. Two-year LR for Rx BED<sub>10</sub> > 105 was 5% vs 19% for < 105 Gy (p<0.01). GTV size was associated with LR on univariate analysis as a continuous variable (p=0.05) with 2-year LR of 5% for < 2.7 cm vs 12% for ≥ 2.7 cm (p=0.01).

PTVmean BED<sub>10</sub> (p<0.01) and GTV size (p=0.04) were independent predictors on multivariate analysis as continuous variables. PTVmean BED<sub>10</sub> was also associated with distant metastasis on univariate and multivariate analysis, but not overall survival.

## Conclusion

There are clear dose-response and tumor volume-response relationships for local control of NSCLC following image-guided SBRT with possible optimal PTVmean BED<sub>10</sub> of > 125 Gy in this dataset.