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, 12.5 Gy x 5, 7.5 Gy x 3, 7.5 Gy x 8 (median=54 Gy, 3 fractions). Median prescription (Rx) BED10=132 Gy (60-180). Median values (Gy) of 3D planned doses for BED 10 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 BED10 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 and was 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 BED10 of > 125 Gy in this dataset.

PTVMean BED10 (p<0.01) and GTV size (p=0.04) were independent predictors on multivariate analysis as continuous variables. PTVmean BED10 was also associated with distant metastasis on univariate and multivariate analysis, but not overall survival.