AbstractID: 6873 Title: A generalized Lyman model incorporating censored time-to-toxicity data and non-dosimetric risk factors

Purpose: In analyzing radiation toxicity, clinical factors and occurrence times of toxicity may be of significance. Yet these factors are not incorporated into the conventional Lyman NTCP model. The purpose of this work was to generalize the Lyman model, incorporating censored time-to-event data and clinical risk factors in addition to dose-volume effects, and to apply the model to analysis of radiation pneumonitis (RP).

Method and Materials: Clinical data were collected from lung cancer patients treated with radiotherapy from 1999 to 2005. Grade $\geq$ 3 RP was the normal tissue endpoint, censored at patient death or last follow-up for patients without RP. Multivariate analyses were used first to identify significant clinical risk factors for RP that were independent of dosimetric quantities. A generalized version of the Lyman model was then developed that included important clinical factors and the distribution of RP times.

Results: Among the 567 patients available for analysis, the crude incidence of grade $\geq$ 3 RP was 21% (118 cases), occurring mainly within the first 8 months post-therapy, when many patients succumb to disease. Smoking habits and dose-volume parameters were found to affect the risk of RP. The generalized Lyman model provided a significantly better fit to data when smoking was taken into account (P=0.005). The estimated lung-volume effect (the parameter n in the Lyman model) was found to be 0.54, but was not significantly different from n=1, consistent with the importance of mean lung dose on the risk of RP. The generalized model predicted NTCP values that were up to 22 percentage points different from those estimated from a fit of the standard Lyman model.

Conclusion: Inclusion of non-dosimetric factors and time-to-event data can significantly impact the predictions of NTCP models that have been based historically solely on dose-volume effects.