

# Active Smoking Is Not Associated with Increased Radiation-Induced Toxicity in Locally Advanced Lung Cancer Patients

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## PURPOSE / OBJECTIVE(S)

To limit morbidity from thoracotomy and improve healing, surgeons often will not operate on active smokers.

Active smoking during radiation therapy is associated with worse tumor control outcomes. However, the relationship between smoking and toxicity of thoracic radiation treatment (TRT) is not well known.

Several studies have suggested that ongoing smoking may have a protective effect against radiation pneumonitis.<sup>1,2</sup> However, other studies have found heavy smoking history to be predictive of radiation pneumonitis.<sup>3,4</sup>

**We conducted this study to determine whether smoking increases the morbidity of thoracic radiation therapy in locally advanced lung cancer patients.**

## MATERIAL & METHODS

Two large prospective databases were analyzed, including from 4 institutional investigator initiated trials (IIT) and a large multicenter statewide quality consortium.

Smoking status was defined as active smokers versus former/never smokers.

Logistic regression was used to determine the relationship between smoking and esophagitis, pneumonitis, and cardiac events.

Adjustments were made for PTV volume, concurrent chemotherapy, and radiation dose to organs at risk. Due to heterogeneity in consortium data follow-up time, weighting variables were used to model pneumonitis outcome.

## RESULTS

Table 1

	Consortium	IIT
Number of pts	1076	172
Mean age (years)	67	66
Mean PTV volume (mL)	359	421
Chemotherapy rate (%)	83.3	69.8
Active smoking rate (%)	40.7	41.9
Grade≥2 pneumonitis incidence (%)	9.2	17.1
Grade≥2 esophagitis incidence (%)	58.7	41.4

Table 2

Clinical variable	Esophagitis			
	Consortium		IIT	
	Odds ratio (OR)	p-value (p)	OR	p
PTV volume	0.996	0.87	0.978	0.75
Concurrent Chemo	2.48	<0.0001	8.64	0.05
Mean Esophageal Dose	1.07	<0.0001	1.06	0.02
Active Smoker	1.19	0.12	1.46	0.35

Table 3

Clinical variable	Pneumonitis				Cardiac Events	
	Consortium		IIT		IIT	
	OR	p	OR	p	OR	p
PTV volume	1.06	0.17	1.01	0.90	0.967	0.71
Concurrent Chemo	1.08	0.87	0.807	0.79	6.24	0.1
Mean Lung Dose	1.07	0.1	1.17	0.05	-	-
Mean Heart Dose	-	-	-	-	1.03	0.29
Active Smoker	0.827	0.49	0.793	0.65	0.954	0.93

A total of 1248 patients were analyzed in the IIT and consortium cohorts (Table 1).

There was no evidence supporting a significant effect of smoking on any toxicity outcome (Tables 2-3).

In both cohorts there was a significant relationship between esophagitis and concurrent chemotherapy use and mean esophageal dose, (p≤0.05).

There was a trend towards significance between mean lung dose and pneumonitis in the IIT cohort (p=0.05).

There was no significant relationship between any variable and cardiac events in the IIT cohort; however, median follow-up was limited to 25.8 months.

## SUMMARY / CONCLUSION

As an independent variable, active smoking is not associated with higher rates of radiation-associated esophagitis, pneumonitis, or cardiac events in locally advanced lung cancer patients.

While smoking cessation remains imperative to improve local control and survival outcomes in lung cancer, our study is the largest prospective data analysis of locally advanced lung cancer patients to show no increase in TRT-induced morbidity in smokers.

**We found that lung cancer patients who are actively smoking do not have increased morbidity from thoracic radiation therapy.**

**However, patients should still be counseled about the importance of smoking cessation.**

**Treatment-related factors (organ dose and concurrent chemo) rather than smoking status seem to drive toxicity development.**

## REFERENCES / ACKNOWLEDGEMENTS

- Jin H, Tucker SL, Liu HH, et al. Dose-volume thresholds and smoking status for the risk of treatment-related pneumonitis in inoperable non-small cell lung cancer treated with definitive radiotherapy. *Radiother Oncol* 2009; 91(3):427-432.
- Hernando ML, Marks LB, Bentel GC, et al. Radiation-induced pulmonary toxicity: A dose-volume histogram analysis in 201 patients with lung cancer. *Int J Radiat Oncol Biol Phys* 2001; 51(3):650-659.
- Li F, Zhou Z, Wu A, et al. Preexisting radiological interstitial lung abnormalities are a risk factor for severe radiation pneumonitis in patients with small-cell lung cancer after thoracic radiation therapy. *Radiat Oncol*. 2018 May 2;13(1):82.
- Baker R, Han G, Sarangkasiri S, et al. Clinical and dosimetric predictors of radiation pneumonitis in a large series of patients treated with stereotactic body radiation therapy to the lung. *Int J Radiat Oncol Biol Phys*. 2013 Jan 1;85(1):190-5.