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# Time Interval Between Staging FDG Positron Emission Tomography (PET) and Initiation of Stereotactic Lung Radiotherapy (SBRT) Impacts the Risk of Recurrence and Metastasis in Non-small Cell Lung Cancer (NSCLC)

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## Background

To study influence of time interval from staging PET scanning to RT start time on recurrence and survival in patients with NSCLC undergoing lung SBRT.

## Methods

Four-hundred eleven patients were treated with lung SBRT for T1-T2N0M0 NSCLC at 5 international institutions using online cone-beam CT (CBCT) image-guided radiotherapy (Elekta Oncology CBCT) from the period 1998 to 2009. Eight percent (8%) of patients had a synchronous primary tumor and 62% of tumors were biopsy-proven. All patients were staged with a diagnostic CT scan; 84% also had FDG-PET and 5% had CT, PET and mediastinoscopy. Sixty-eight percent (68%) had T1N0 tumors, 30% T2N0 and 1% were locally recurrent after surgery. The median maximum tumor dimension was 2.4 cm (range 0.9-8.5cm). Patients were treated with a variety of prescription doses according to each institution's protocol. The most common fractionation schedules were: 18-20Gy x 3; 12Gy x 4; 12Gy x 5; and 12.5Gy x 3 (median dose 54 Gy, 3 fractions). Mean follow-up time=1.3y.

## Results

Median time from PET to SBRT was 5.7 weeks (wks) (0-30.4 wks); median number of days elapsed during RT was 8d. Thirteen percent (13%) of patients underwent PET  $\leq$  2 wks of SBRT, while 76% underwent PET  $\leq$  8.5 wks of SBRT. The median time from mediastinoscopy to SBRT was "x" wks (range). For all patients, 1y overall survival (OS) and cause specific survival (CSS) were 83% and 94%, and at 2y 64% and 91%, respectively. Two years OS and CSS for patients who underwent PET staging were 62% and 87% compared to

44% and 74% for those who did not ( $p=0.03, 0.04$ , respectively). There were no differences in local recurrence (LR) or regional recurrence (RR) for patients undergoing staging PET vs. no PET ( $p=NS$ ); LR 7% vs 8%, RR 9% vs 13%. However, DM was substantially higher in those without staging PET vs. those with staging PET (37% no PET vs. 22% PET,  $p=0.007$ ), as was the risk of death (Hazard ratio 1.53 for no PET,  $p=0.03$  Cox regression). Although the mere staging presence of PET did not impact the risk of RR, the time from staging PET to SBRT predicted both RR and DM, with a trend for predicting death on multivariate analysis ( $p=0.1$ ). Patients undergoing PET  $\leq$  8.5 wks from PET to SBRT start. A time interval  $>8.5$  wks from PET to SBRT start doubled the risk of DM from 18% to 37% ( $p=0.02$ ). No statistically significant differences existed in any recurrence or survival endpoints for patients undergoing vs. not mediastinoscopy.

## Conclusion

The use of staging PET prior to SBRT for NSCLC improved OS and CSS and substantially reduced DM and death. A time interval  $>8.5$  weeks between staging PET and initiation of SBRT increased the risk of RR and DM. The results of this analysis substantiate the importance of staging PET for NSCLC patients treated curatively with SBRT and emphasize the importance of timely staging for optimal outcomes.