# Initial Tumor Metabolic Parameters (Maximum SUV and Metabolic Volume) Predict Death From Lung Cancer and Rapid SUV Decline is Associated with Local Control

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## Rationale and Objectives

- Factors associated with local failure and death from lung cancer were evaluated based on post-treatment FDG-PET imaging in patients (pts) with non-small cell lung cancer (NSCLC).

- PET-CT scans were obtained 6-8 weeks after thoracic RT and approximately every 3 months thereafter.

## Materials and Methods

- **Patient Population:** 50 pts with NSCLC who received thoracic RT (with or without chemotherapy) between 2004-2008 were eligible if they had pre-RT PET scan and at least one post-RT PET scan.

- **Methods:** Primary tumor and hypermetabolic lymph nodes included in the RT field were contoured on the initial and post-treatment PET scans applying a gradient "PET edge" technique (Mimvista Corp, Cleveland, OH). PET edge is superior to the percent threshold techniques (i.e. 25%, 30% max SUV etc) (Nelson A et al, ASTRO 2009 abstract #2993) with regard to reflecting true tumor volume.

- Maximum SUV (MaxSUV) and the Metabolic Tumor Volume (MTV) of the primary tumor and involved lymph nodes were measured using the same software.

- **Statistics:** MTV and Max SUV were assessed longitudinally, providing for each patient separate log transformed initial estimates and changes (value at time 0 - value at time 1). Competing risks analysis of time to local failure and death were completed using the methods of Gray (Gray RJ, J Ann Stat 1988; 16:1141–1154.), as implemented in the R package CMPRSK. Results are reported as hazard ratios, 95% confidence interval of hazard ratio, and 2-sided p-values.
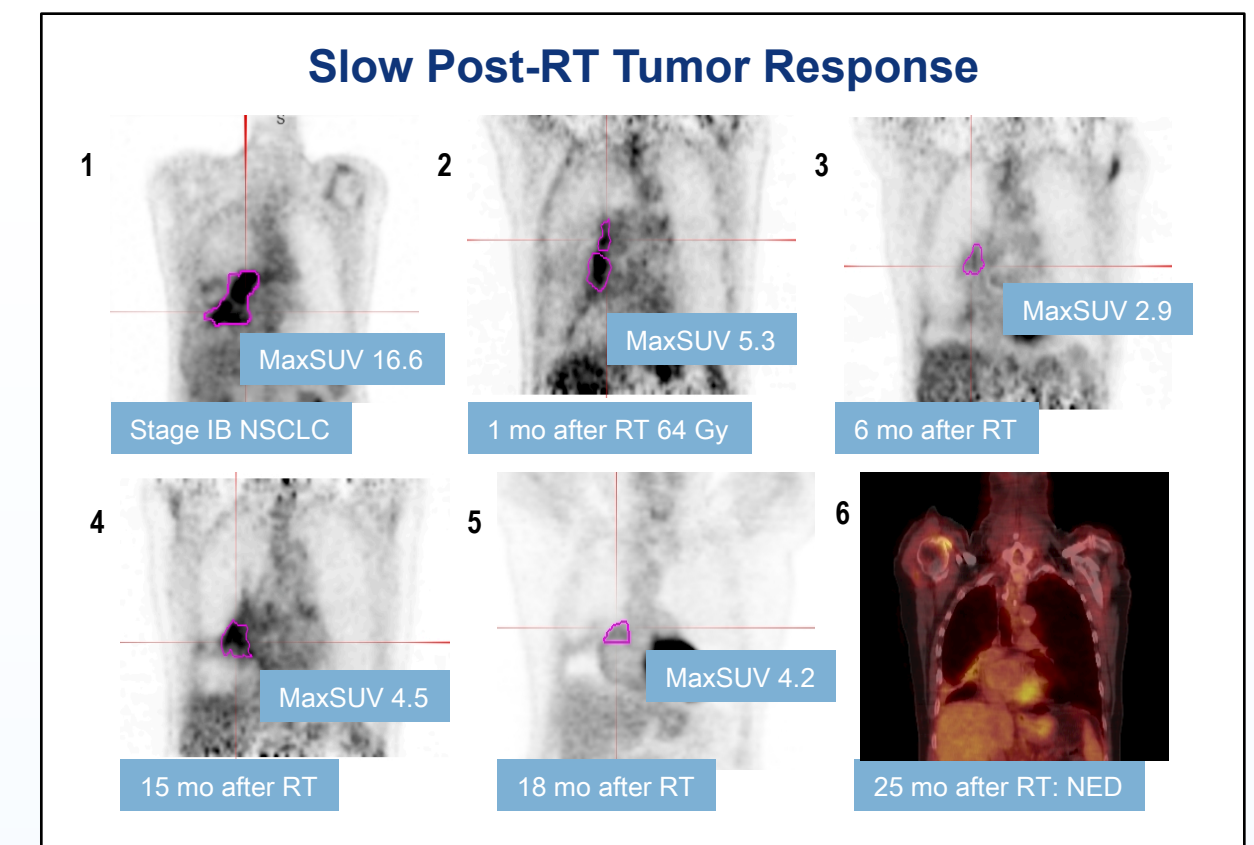
## Results: Patient Characteristics

| Characteristic | Number (range) |
|---|---|
| Gender F:M | 33 : 17 |
| Median age | 63 |
| Stage:    I | 5 |
| III | 29 |
| IV | 11 |
| recurrent | 5 |
| Median RT dose | 60 (range 35-71) |
| BED dose | 73.2 |
| Number of pts with post-RT PET scans | 50 (1 PET scan) |
| | 26 (2 scans) |
| | 11 (3 scans) |
| | 4 (4 scans) |
| | 4 (5 scans) |
| | 3 (6 scans) |

## Results

- A total of 262 primary tumors and/or lymph nodes were analyzed.

- Median FU time: 14.2 mo (range 2-52.2)

- Metabolic complete response (mCR, SUV≤2.5) was achieved in 38% patients. LF occurred in 10 pts.

- The primary tumor median MaxSUV declined by 72% by the 1st post-RT PET; 76% by the 2nd and 77% by the 3rd.

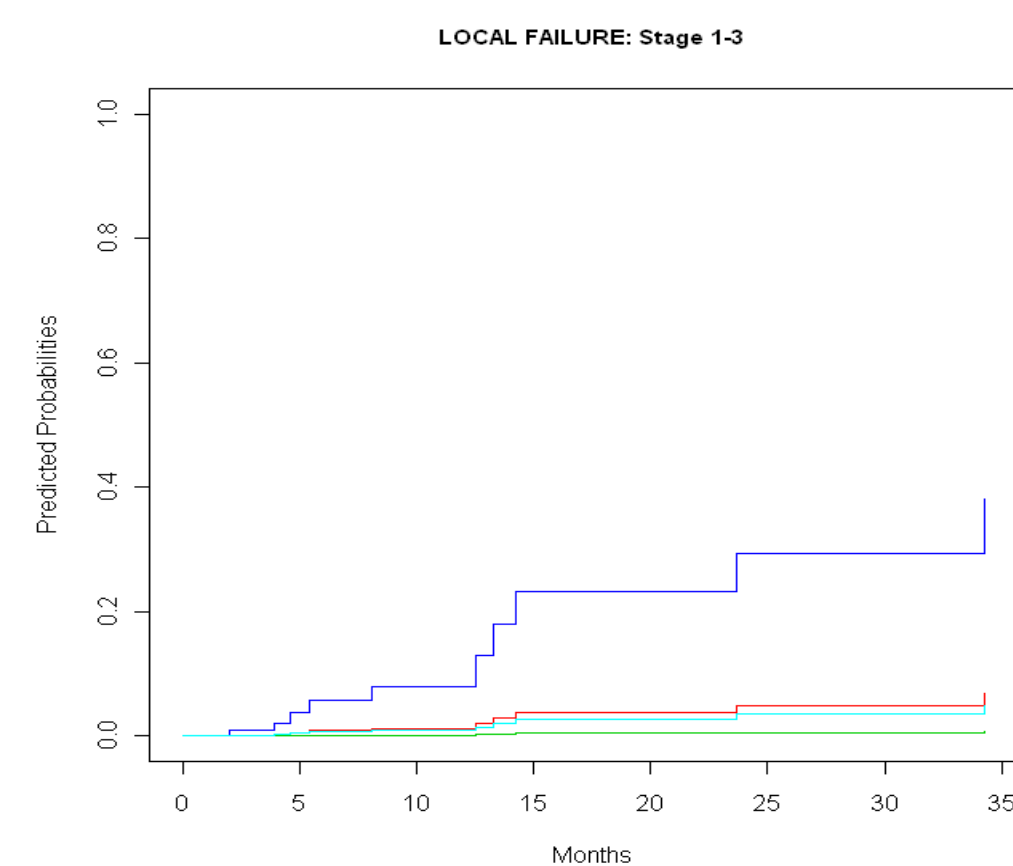- Median time to local failure (LF) not reached (75th %: 24 mo); MST 31 mo.

## Results: Metabolic Response After RT

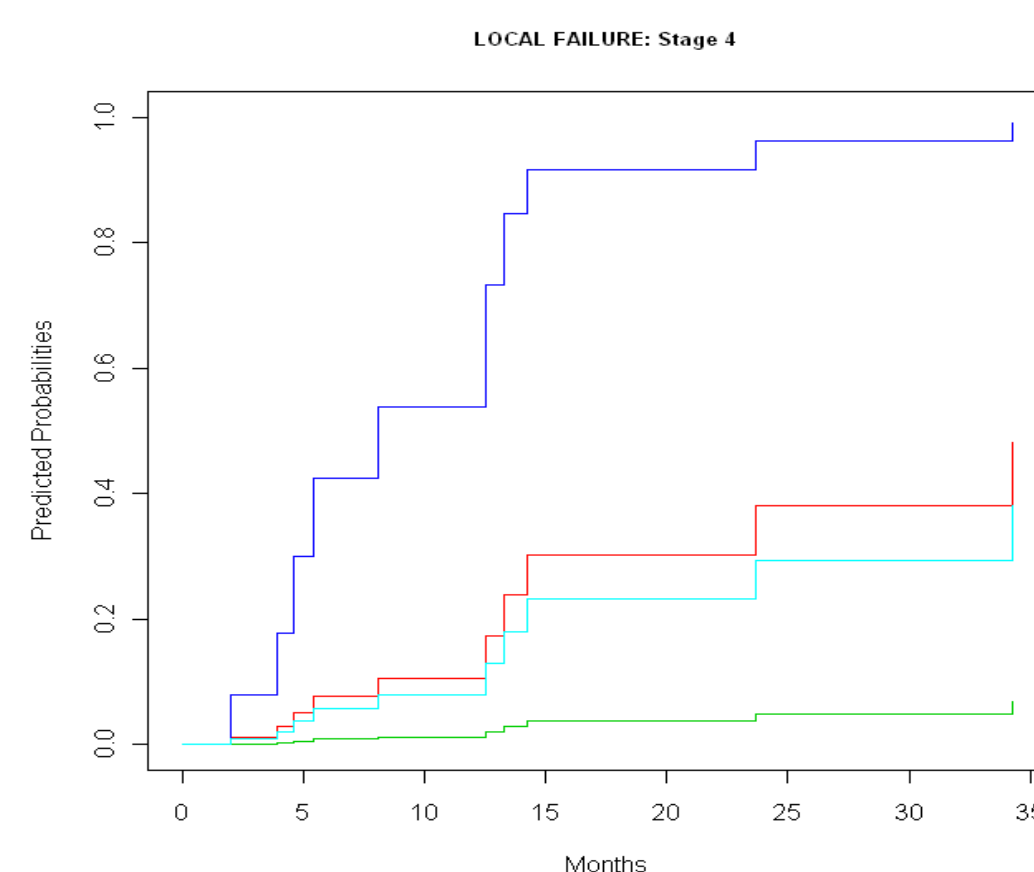| Metric | Pre-RT | Post-RT #1 | Post-RT #2 |
|---|---|---|---|
| Tumor Max SUV | **12.3 (1.9-31)** | 3.4 (0.9-20.9) | 2.9 (1-22.5) |
| Lymph nodes Max SUV | 9.1 (2-23.7) | 2.8 (1.5-7.9) | 2.8 (1.5-8.9) |
| MTV (tumor + lymph nodes) | 51.1 cc (1.5-491) | 37.3 cc (3-585) | 22.9 cc (2-153) |

### Fig.1. Local failure in Patients with Stages I-III

Local failure was defined as increase in MaxSUV of either the primary tumor or lymph nodes in the RT field, with any accompanying increase in size of the tumor on a CT scan.



### Fig.2. Local failure in Patients with Stage IV



**Legend to Figures 1 and 2:**
Blue = hi change in MTV, low change in SUV
Red = low change in MTV, low change in SUV
Turquoise = high change in MTV, high change in SUV
Green =low change in MTV, high change in SUV

### Slow Post-RT Tumor Response



## Variables Associated with Local Failure: Multivariate Analysis

| Variable | HR | p-value |
|---|---|---|
| Age | 0.98 | 0.46 |
| Sex (F/M) | 0.81 | 0.76 |
| Stage | 15.35 | 0.009 |
| BED RT total dose Lo/Hi1 | 2.15 | 0.31 |
| Pre-treatment MTV | 3.45 | 0.19 |
| Change in MTV (continuous) | 10.45 | 0.057 |
| Pre-treatment SUV | 5.9 | 0.44 |
| Change in SUV | 0.082 | 0.045 |

## Variables Associated with Death: Multivariate Analysis

| Variable | HR | p-value |
|---|---|---|
| Age | 1.035 | 0.17 |
| Sex (F/M) | 6.21 | 0.11 |
| Stage | 1.44 | 0.79 |
| BED RT total dose Lo/Hi | 0.29 | 0.31 |
| Pre-treatment MTV (categor.) | 6.36 | 0.016 |
| Change in MTV | 0.24 | 0.11 |
| Pre-treatment SUV (contin.) | 1.05 | 0.037 |
| Change in SUV | 0.54 | 0.79 |

## Conclusions

- LF after thoracic RT is not common (20%) during lifetime of pts receiving 3D thoracic RT and the rate of metabolic response is rapid.

- Higher pre-treatment maximum SUV and MTV>51 cc are associated with increased risk of death from lung cancer.

- Rapid post-treatment decline in SUV on first follow-up PET scan is associated with subsequent lower risk of local failure.

- However, the decline in MTV was paradoxically associated with eventual increased failure. We hypothesize this may be related to the aggressive tumors which respond quickly yet recur faster.

- Patients with Stage IV lung cancer are more likely to experience local failure than lower stage patients, which may be due to the lower thoracic RT doses.