Conclusion: Core biopsy with a biopsy gun increase the diagnostic accuracy with a higher histologic predictive rate and no obvious additional risk of complications.

P1-082 **Imaging and Staging Posters, Mon, Sept 3**

Metabolic tumor volume predicts disease progression and overall survival in lung cancer

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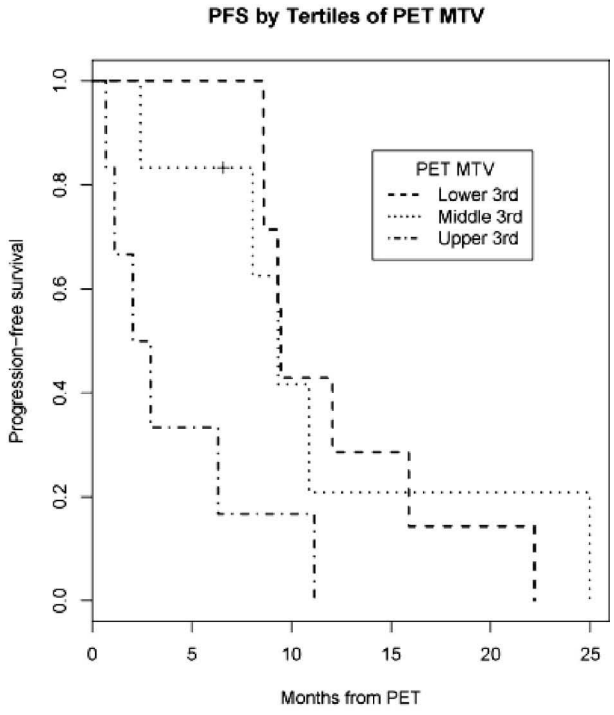
Background: In lung cancer, stage has classically been the most important prognostic factor for disease progression and survival. However, stage may be simply a surrogate for underlying tumor burden. The purpose of this study was to assess the prognostic value of pre-treatment tumor volume as measured by FDG-PET imaging.

Methods: We identified a cohort of 19 patients with lung cancer who had staging PET-CT scans prior to any therapy, and adequate follow-up. Follow-up was complete to the time of progression for 18 of 19 patients, and to the time of death for 15 of 19 patients. Four patients remain alive. We used custom software to segment metabolically active tumor regions semi-automatically on PET scans. We determined the relationship between time to progression (TTP) and two PET parameters: total metabolic tumor volume (MTV), and standardized uptake value (SUV).

Results: The median TTP for the cohort was 8.6 months (range 0.7-25). The median overall survival (OS) was 15 months. The median MTV was 27 mL. On multivariate Cox proportional hazards regression analysis, an increase in MTV of 25 mL (the difference between the 75th and 25thpercentiles) was associated with a 2.6 fold increase in hazard of progression, statistically significant (p=0.023) after controlling for stage, age, KPS, and weight loss. Figure 1 shows the relationship between MTV and progression-free survival. Similarly, an increase in MTV of 25 mL was associated with a 2.9 fold increase in the hazard of death (p=0.0017). We did not find a significant relationship between SUV and TTP or OS.

Conclusions: In this study, high tumor burden assessed by PET MTV is a poor prognostic feature in lung cancer independent of stage, age, KPS, and weight loss. This may be promising for stratifying patients in randomized trials, and ultimately for selecting risk-adapted therapies. These results will need to be validated in larger cohorts with longer follow-up, as well as evaluated prospectively.

Figure 1



P1-083 **Imaging and Staging Posters, Mon, Sept 3**

Usefulness of fluorodeoxyglucose positron emission tomography integrated with computed tomography (FDG-PET/CT) in determining the resectability of primary lung cancer

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Background: The integration of computed tomography (CT) and FDG-PET provides better specificity and sensitivity in tumor imaging than either component alone. We prospectively evaluated FDG-PET/CT as a method for determining surgical indications in patients with primary lung cancer.

Methods: Consecutive patients with a diagnosis of primary lung cancer based on preoperative cytology or histologic examination in our hospital were enrolled prospectively. Conventional disease staging was performed using chest CT, abdominal CT, brain magnetic resonance imaging (MRI), and bone scintigraphy. Treatment strategy was determined based on conventional staging. Independently, simultaneous PET-staging was performed based on whole body FDG-PET/CT and brain MRI. Results of preoperative PET were compared with surgical specimens of hilar and mediastinal lymph nodes. In nonsurgical cases, node (N) and metastasis (M) factors diagnosed by PET were evaluated based on the clinical course or results from biopsy specimens of specific sites.

Results: Twenty men and 22 women, age range, 47 to 87 years (71±10, mean±SD), were enrolled. Histology included 27 adenocarcinomas, 10 squamous cell carcinomas, and 5 small cell carcinomas. Clinical stage by conventional staging was c-stages IA or B in 13, IIA or B in 3, IIIA in 6, IIIB in 7, and IV in 13. According to the conventional staging, 16 patients underwent surgery. By PET-staging, 9 cases (21%) were

up-staged and 2 cases (5%) were down-staged. In patients with staging discrepancy, PET-staging was accurate in 8 cases including undetected M1 disease, and conventional staging was accurate in 3 cases, based on overdiagnosis of N factor by PET. Synchronous malignant diseases (laryngeal cancer and malignant lymphoma) were detected by PET. One bronchioloalveolar carcinoma showing focal ground-glass opacity on CT was PET negative. PET correctly identified surgical candidates in 13 of 42 cases. In resected cases, one false negative (6%) and 3 false positive (19%) lymph node metastases were diagnosed by PET. Since the false negative case was microscopic N2 limited to one station, curative operation was performed. If we considered PET cN3 disease as a surgical contraindication, one surgical candidate would have been denied surgery. Maximum standardized uptake value (maxSUV) of all primary lesions ranged from 0 to 23.0 (8.1±4.3, mean±SD). The maxSUV among surgical cases (6.3±3.5) was smaller than among nonsurgical cases (9.3±4.4, $p<0.05$). The maxSUV was similar among the different histologic types.

Conclusions: FDG-PET/CT is useful for determining the clinical stage and resectability of primary lung cancer. However, false positive findings in regional lymph nodes, possibly due to past infectious diseases, are of major concern to be solved. A negative PET study in lymph nodes and distant metastases suggests that these patients can proceed directly to thoracotomy without mediastinoscopy. The maxSUV was related with resectability of primary lung cancer.

P1-084 **Imaging and Staging Posters, Mon, Sept 3**

Mammalian target of rapamycin (mTOR) inhibition by RAD001 in patients (pts) with reccurent non-small cell lung cancer (NSCLC): Use of 18F fluorodeoxyglucose positron-emission tomography (FDG-PET) in evaluation of the pharmacodynamic effect

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Background: RAD001 (everolimus) is a novel inhibitor of mTOR formulated for oral administration, currently investigated as an anticancer agent in clinical studies. In preclinical experiments a prominent impact of mTOR inhibition on glucose homeostasis was described with the transcription factor HIF-1 as one of the primary mediators of RAD001-induced inhibition of mTOR. Moreover, the inhibition of FDG uptake has been demonstrated by FDG-PET imaging in preclinical models treated with RAD001. Therefore we reasoned that glucose metabolism as measured by FDG-PET might thus serve as a pharmacodynamic marker of RAD001 acting on its target in cancer pts. Here we report for the first time on the use of FDG-PET in evaluation of the pharmacodynamic effects of RAD001 in pts with recurrent NSCLC.

Patients and Methods: Patients with advanced NSCLC previously treated with either chemotherapy only or with chemotherapy and an EGFR inhibitor were treated with 10 mg continuous daily dose of RAD001 in an open label, multi-centre phase II study. A subgroup of 8 pts enrolled in 2 of the study centres was evaluated by serial FDG-PET scans. FDG-PET was performed at the baseline and on the day 8 of treatment in all 8 patients. In addition, in 5 out of these 8 pts FDG-PET was performed on the day 28 of treatment. Evaluation of FDG-PET scans was performed centrally. The sum of the maximum standardized uptake values (sSUVmax) measured in up to 5 lesions was calculated at each time point. Percentage change of sSUVmax values from baseline was calculated on days 8 and 28. In addition, standard computed tomography (CT) scans obtained at baseline (8 pts) and on day 28 (6 pts) were evaluated and the change of the sum of the longest diameter of lesions (up to 10 selected lesions including those evaluated by FDG-PET) was calculated. A lesion by lesion analysis will be presented.

Results: Reduction of sSUVmax on day 8 was observed in all pts and ranged between 1.4% and 89.1%. Reduction of sSUVmax on day 28 was less pronounced compared to the reduction on day 8.

Changes in sSUVmax (day 8 and day 28) and changes in sums of longest diameter of lesions evaluated by CT scans are provided in table below.

Patient Number	Change sSUVmax d8(%)	Change sSUVmax d28(%)	Change sumCT d28(%)
0701-0002	-19.4	1.5	3.3
0701-0003	-1.4	NA	NA
0701-0004	-89.1	-82.3	-26.6
0701-0005	-19.2	NA	NA
0601-0001	-52.2	-9.7	77.9
0601-0003	-17.4	NA	12.7
0601-0007	-13.0	-2.9	11.1
0601-0009	-20.6	-12.7	-16.7

NA=Not Available Measurements

Conclusions: Results of this study suggest the value of FDG-PET as a tool for early evaluation of the pharmacodynamic effect of mTOR inhibitors such as RAD001 in patients with NSCLC. In addition, confirmation of similar results obtained in preclinical models suggests the usefulness of FDG-PET in clinical profiling of mTOR inhibitors.

Correlation of early pharmacodynamic changes evaluated by FDG-PET with clinical effects of RAD001 treatment should be evaluated in larger studies.

P1-085 **Imaging and Staging Posters, Mon, Sept 3**

Factors affecting diagnostic accuracy of ct-guided transthoracic needle biopsy of lung lesions: results of 660 consecutive procedures

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Background: CT-guided Transthoracic Needle Aspiration Biopsy (TNAB) is widely used as a diagnostic tool in the diagnostic work-up of thoracic lesions. The reported sensitivity for detection of lung neoplastic lesions with CT-guided TNB varies from 68% to 93% with