Presurgical Staging of Non-small Cell Lung Cancer*

Positron Emission Tomography, Integrated Positron Emission Tomography/CT, and Software Image Fusion

Benjamin S. Halpern, MD; Christiaan Schiepers, MD, PhD; Wolfgang A. Weber, MD; Tyler L. Crawford, MD; Barbara J. Fueger, MD; Michael E. Phelps, PhD; and Johannes Czernin, MD

Purpose: **To compare the diagnostic accuracy of positron emission tomography (PET) and integrated PET/CT and to evaluate the performance of software fusion for staging of non-small cell lung cancer (NSCLC).**
Methods: **Thirty-six patients (17 men and 19 women) with NSCLC underwent staging with integrated PET/CT followed by mediastinal lymph node dissection and tumor resection. Twenty-five of the 36 patients (69%) underwent separate CT studies for software fusion of images. Two blinded reviewers analyzed in consensus all PET images, and an experienced radiologist was added to assess integrated and software-fused PET/CT images. Histopathologic findings served as "gold standard" for determining the diagnostic accuracy of all modalities.**
Results: **Reviewers examining PET and integrated PET/CT classified T stage accurately in 67% (20 of 30 patients) and 97% (29 of 30 patients), respectively ($p < 0.05$). Overall, interpretations based on PET staged 57% (17 of 30 patients) correctly, overstaged 6 patients (20%), and understaged 7 patients (23%). Interpretations based on integrated PET/CT correctly staged 83% (25 of 30 patients), overstaged 3 patients (10%), and understaged 2 patients (7%). The overall staging accuracy of integrated PET/CT was significantly higher than that of PET ($p < 0.05$). Automatic software fusion of separately obtained PET and CT studies was successful in 68% of the patients but failed in 32%. In successful software fusion cases, the results of software fusion with regards to T stage and N stage were not different from integrated PET/CT.**
Conclusions: **Integrated PET/CT compared with PET alone was associated with 26% points-greater overall diagnostic accuracy ($p = 0.01$). The software fusion method failed to provide acceptable coregistration in > 30% of the patients.** ***(CHEST 2005; 128:2289–2297)***

Key words: CT; dual-modality imaging; fusion imaging; positron emission tomography; non-small cell lung cancer

Abbreviations: CI = confidence interval; FDG = fluorodeoxyglucose; FDG-PET = fluorodeoxyglucose positron emission tomography; NS = not significant; NSCLC = non-small cell lung cancer; NPV = negative predictive value; PET = positron emission tomography; PPV = positive predictive value

Lung cancer is responsible for 13% of all new cancers and 28% of all cancer deaths and is the most common cause of cancer deaths in the United States.[1] The prognosis varies according to stage, with 5-year survival rates for stage I of 42%, stage II of 23%, stage IIIA of 11%, stage IIIB of 5%, and stage IV of 1%. Thus, accurate staging of non-small cell lung cancer (NSCLC) provides important prognostic information and determines the best treatment approach.[2]

Fluorodeoxyglucose positron emission tomography (FDG-PET) imaging is the most accurate imag-

*From the Department of Molecular and Medical Pharmacology (Drs. Schiepers, Weber, Fueger, Phelps, and Czernin), Ahmanson Biological Imaging Center, UCLA David Geffen School of Medicine, Los Angeles, CA; Department of Radiological Sciences (Dr. Crawford), UCLA David Geffen School of Medicine, Los Angeles, CA; and Department of Radiology (Dr. Halpern), Medical Diagnostic Division, Medical University Vienna, Vienna, Austria.

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Correspondence to: Johannes Czernin, MD, UCLA School of Medicine, Nuclear Medicine, AR 128 CHS, 10833 Le Conte Ave, Los Angeles, CA 90095-6942; e-mail: jczernin@mednet.ucla.edu

ing modality for lung cancer staging but faces several major challenges. The first is its limited specificity due to increased glycolytic activity of benign tumors and inflammatory tissue, in addition to that of malignant tumors.[3] Secondly, its anatomic resolution is limited, precluding exact localization of glucose alterations to specific anatomic structures. Thirdly, mildly hypermetabolic primary or metastatic lesions might be too small to be identified with FDG-PET. Finally, some malignancies such as pure bronchoalveolar carcinoma may not exhibit any discernible increase in glycolytic activity.

Integrated PET/CT and software fusion of positron emission tomography (PET) and CT images can help to overcome these limitations to a certain degree.[4] With integrated PET/CT, anatomic and molecular information can accurately be coregistered.[5]

Another way to achieve reasonable coregistration between metabolic and anatomic imaging is the software fusion of separately obtained PET and CT images. Software fusion is relatively inexpensive, but to our knowledge, its clinical performance has not been compared to that of integrated PET/CT.

Some studies[6,7] have already compared PET and integrated PET/CT for staging in NSCLC and have demonstrated additional gains in diagnostic accuracy. However, the aim of the current study was to compare the diagnostic accuracy between FDG-PET, integrated PET/CT, and software fusion for the staging of NSCLC.

Materials and Methods

Patient Population

Since the introduction of integrated PET/CT at our institution in August 2002, a total of 289 patients with biopsy specimen-proven or suspected NSCLC were evaluated in our institution. Of these, 36 patients (12%) were identified in whom complete lymph node staging or complete lymph node staging plus thoracotomy was performed (17 men and 19 women; mean age ± SD, 68 ± 10 years; range, 46 to 83 years). Integrated PET/CT was performed within 16 ± 12 days prior to surgery or mediastinoscopy. Histologic study revealed adenocarcinoma in 18 patients, adenocarcinoma with mixed cellularity in 7 patients, squamous cell carcinoma in 7 patients, pure bronchoalveolar carcinoma in 2 patients, and large-cell carcinoma in the 2 remaining patients.

PET/CT Imaging Protocol

All patients were advised to fast for at least 6 h prior to the integrated PET/CT examination. Sixty minutes prior to the integrated PET/CT scan, all patients received 7.77 megabecquerels per kilogram of fluorodeoxyglucose (FDG). Patients were scanned from the mid-thigh level to the base of the skull in the "arms-up" position. CT studies were performed without IV contrast application. All patients were advised not to speak, chew, or move during the uptake period of FDG and the scan.

Integrated PET/CT studies were acquired with a scanner (Biograph Scanner; Siemens Medical Solutions; Hoffman Estates, IL). This system consists of an ECAT ACCEL PET system (CTI; Knoxville, TN), without septa and transmission sources, and a Somatom Emotion duo radiograph CT system (Siemens Medical Systems; Iselin, NJ).

After determining the imaging field, a 80- to 110-s whole-body CT acquisition was performed using the following parameters: 130 kilovolt peak, 120 mA, 1-s tube rotation, 4-mm slice collimation, 5-mm reconstruction slice thickness, and a table feed of 8 mm per rotation (*ie*, pitch = 2). All studies were performed at shallow breathing. On completion of the CT portion, the PET emission data were acquired in the three-dimensional mode using a weight-based protocol as described previously.[8]

PET/CT Image Reconstruction

CT images were reconstructed using conventional-filtered back-projection at 3.4-mm axial intervals to match the slice separation of the PET data. PET images were reconstructed using iterative algorithms (ordered-subset expectation maximization, two iterations, eight subsets) to a final image resolution of 8.8-mm full width half maximum. For attenuation correction, CT Hounsfield units were mapped to the linear attenuation coefficients of 511 keV.[5,9]

Software PET and CT Image Fusion

Twenty-five of the 36 patients (69%) underwent separate noncontrast CT scans within 6 weeks of the integrated PET/CT study. No therapeutic interventions were performed between the integrated PET/CT and the separate CT study. CT studies were performed with a spiral CT scanner (HiSpeed Spiral CT/I; GE Medical Systems; Milwaukee, WI) using the following parameters: 130 kilovolt peak, 80 mA, 0.8-s tube rotation, 2.5-mm slice collimation, 3-mm reconstruction slice thickness, and a table feed of 10 mm per rotation (*ie*, pitch = 2). All studies were performed at breath-holding during maximal inspiration.

Software fusion of PET emission data and CT was performed using a fully automated commercially available software approach (Mirada Solutions; Oxford, UK). This approach is based on similarity measures corresponding to different modeling assumptions, such as correlation coefficient, correlation ratio, and mutual information.[10] After loading the PET and CT data, a linear rigid fusion was applied first. The linear algorithm is limited to translation, rotation, and scaling of the images.[11,12] This was followed by a nonlinear fusion algorithm. This approach, also known as image warping, allows for corrections of configuration changes, as for instance induced by breathing or movement of internal organs.[12] No manual alignment of images was used since this approach is known to be unreliable because of the adjustment of multiple parameters.

To determine the degree of misalignment between PET and CT both for hardware and software fusion, the center of hypermetabolic lesions (*ie*, lung tumors or lymph nodes) was depicted as landmarks on CT or PET images. Successful software fusion was defined as coregistration of the hypermetabolic region on PET to a distance of < 2 cm in the x, y, and z directions of the anatomically localized lesion on CT. The distance of 2 cm was chosen because this represents two times the size of lymph nodes deemed positive by CT and approximately two times the PET scanner resolution after image reconstruction. Therefore, a misalignment of 2 cm was considered to be of clinical relevance for successful software fusion. PET and CT foci were then measured in the x, y, and z directions, and the overall distance (D) between landmarks on PET and CT was calculated using the following formula: