GENERAL THORACIC SURGERY

MEDIASTINAL LYMPH NODE STAGING OF NON-SMALL-CELL LUNG CANCER: A PROSPECTIVE COMPARISON OF COMPUTED TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY

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We compared the abilities of positron emission tomography and computed tomography to detect N2 or N3 lymph node metastases (N2 or N3) in patients with lung cancer. Positron emission tomography detects increased rates of glucose uptake, characteristic of malignant cells. Patients with peripheral tumors smaller than 2 cm and a normal mediastinum were ineligible. All patients underwent computed tomography, positron emission tomography, and surgical staging. The American Thoracic Society lymph node map was used. Computed and positron emission tomographic scans were read by separate radiologists blinded to surgical staging results. Lymph nodes were "positive" by computed tomography if larger than 1.0 cm in short-axis diameter. Standardized uptake values were recorded from areas on positron emission tomography corresponding to those from which biopsy specimens were taken; if greater than 4.2, they were called "positive." Seventy-five lymph node stations (2.8 per patient) were analyzed in 27 patients. Computed tomography incorrectly staged the mediastinum as positive for metastases in three patients and as negative for metastases in three patients. Sensitivity and specificity of computed tomographic scans were 67% and 83%, respectively. Positron emission tomography correctly staged the mediastinum in all 27 patients. When analyzed by individual node station, there were four false positive and four false negative results by computed tomography (sensitivity = 60%, specificity = 93%, positive predictive value = 60%). Positron emission tomography mislabeled one node station as positive (100% sensitive, 98% specific, positive predictive value 91%). The differences were significant when the data were analyzed both for individual lymph node stations ($p = 0.039$) and for patients ($p = 0.031$) (McNemar test). Positron emission tomography and computed tomography are more accurate than computed tomography alone in detecting mediastinal lymph node metastases from non-small-cell lung cancer. (J THORAC CARDIOVASC SURG 1996;111:642-8)

Computed tomography (CT) is commonly used for preoperative assessment of the mediastinum in patients with non-small-cell lung cancer (NSCLC).¹ However, in many recent studies, the sensitivity and specificity of CT for detecting the presence or absence of mediastinal lymph node metastases in these patients was low (60% to 65%).^{2,3} CT detec-

tion of lymph node metastases in patients with NSCLC is based on lymph node size criteria, with lymph nodes greater than 1 cm in short-axis diameter generally considered to contain metastases.³ Positron emission tomography (PET) detects increased rates of glucose metabolism, characteristic of malignant cells, by measuring the uptake of a

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positron-emitting glucose analog [2-18F]fluoro-2-deoxy-D-glucose (FDG).^{4,5} FDG-PET can differentiate malignant from benign lung tumors⁵⁻⁷ and can detect the presence of metastases from primary lung cancers to mediastinal lymph nodes^{7,8} and scalene lymph nodes.⁹ The aims of the current study were (1) to confirm the ability of FDG-PET to accurately predict the presence or absence of mediastinal lymph node metastases in patients with NSCLC, with histologic analysis of lymph node tissue in all patients used as the gold standard, (2) to develop semiquantitative methods (standardized uptake values, SUVs) for analyzing the information contained in FDG-PET images, and (3) to prospectively evaluate the ability of FDG-PET supplemented by CT to detect mediastinal lymph node metastases in patients with lung cancer compared with the ability of CT to do so.

Patients and methods

We prospectively compared the ability of FDG-PET and of CT to detect regional lymph node metastases in 27 patients with known or suspected NSCLC. Patients were excluded from analysis (1) if they were not appropriate candidates for mediastinoscopy or thoracotomy or (2) if the only abnormality on chest CT scan consisted of a solitary pulmonary nodule 2 cm in diameter or less without CT evidence of mediastinal lymph node enlargement. All patients who agreed to participate in the trial gave written informed consent. The protocol was approved by the institutional review boards at the participating institutions.

CT. The CT scans were obtained on a General Electric (Brookfield, Wis.) 9800-Hilite-HTD scanner. Routine images were obtained to the level of the adrenal glands, with 10 mm collimation at 10 mm table increments, using 120 kV, 120 mA, 2-second scans reconstructed with standard algorithms. Isovue 300 (iopamidol 61%) was used for intravenous contrast enhancement and was infused at a rate of 0.5 ml/min for 60 seconds, then increased to 1.5 ml/min to a complete infusion of 140 ml for the total volume. CT was performed before PET in all patients.

PET. A Siemens/CTI ECAT 931 positron emission tomograph (CTI, Knoxville, Tenn.) with a 12 cm axial field of view was used for all patients. FDG was synthesized according to standard methods with the Siemens/CTI chemical processing control unit and radioisotope delivery system. Quality control tests were performed on-site. The purity of FDG exceeded 95% for all doses. The total FDG dose ranged from 9.5 to 11 mCi.

Images were acquired by means of the following protocol. Patients took nothing orally for at least 4 hours. Informed consent was obtained. A rectilinear transmission scan was acquired to aid in positioning the patient after inspection of a plain chest radiograph or CT scan to determine the location of the lung mass. A 0.5 ml sample of blood was drawn for determination of the baseline blood glucose level (no manipulation of the blood glucose

level was done) and the data were recorded. The FDG was administered intravenously. After a 60-minute uptake period, the patient was positioned in the scanner once again. An emission scan was acquired at 20 minutes for each bed position (an image of the thorax requires two bed positions on average) for a total of 40 minutes. Image reconstruction done by measured attenuation correction was performed by means of a Hann filter with 0.5-pixel cutoff. The transaxial images were reconstructed into sagittal and coronal planes.

Interpretation of studies. CT scans were interpreted by one radiologist (J.T.) who had no knowledge of the identity of the patient, the findings of surgical staging procedures, or the results of other imaging studies. Mediastinal lymph nodes were localized according to the lymph node map proposed by the American Thoracic Society.¹⁰ Regional lymph nodes were considered to contain metastatic tumor if they were greater than 1.0 cm in short-axis diameter. The size and location of the primary tumor, as well as the presence of postobstructive atelectasis, mediastinal invasion, chest wall invasion, pleural effusion, or other pertinent findings, were recorded on standardized data sheets. Any abnormalities of the bones, liver, or adrenal glands were also recorded.

FDG-PET scans were interpreted by one nuclear medicine physician (L.G.). The corresponding CT scan was available for review by this physician when the PET was interpreted. The nuclear medicine physician did not know the identity of the patient, the findings of surgical staging, or the results of imaging studies other than CT. PET images were displayed in Imagetool on a Sun microsystems SparcStation 1+ using axial planes (Sun Microsystems, Mountain View, Calif.). Co-registration of CT and PET images was not performed. CT was used to define the location of specific areas of increased FDG uptake seen on PET, which were thought to represent either the primary malignant tumor or regional metastases. These areas were generally characterized as being focal, spherical regions where the FDG uptake was increased over that of the immediately adjacent tissue. Streaky or linear areas, focal areas with FDG uptake similar to that of the surrounding tissue, and areas near the base of the heart (where normally high rates of glucose uptake by atrial tissue can be measured) were not generally considered to represent malignant tissue. As used throughout this report, the phrase *mediastinal FDG uptake* refers to FDG uptake by *noncardiac tissue*. Symmetrical areas of FDG uptake near areas of skeletal muscle or the thyroid gland were not indicative of malignant tissue.

A semiquantitative analysis was performed. The amount of FDG uptake in a given region was converted into a unitless number, the SUV. The SUV normalizes the amount of FDG uptake for the body weight of the patient and the specific dose of FDG injected. The maximum radionuclide concentration for a given region (maximum FDG uptake expressed as microcuries per milliliter [$\mu\text{Ci/ml}$]) was identified. That number was then converted into the SUV for that region by the formula: $\text{SUV} = (\mu\text{Ci/ml}) \cdot (\text{kg/mCi})$. No recovery coefficient or glucose correction was applied.

Because the "background," or normal, amount of glucose uptake varies for different regions in the chest,

Table I. Mediastinal lymph node status by CT, analyzed according to patient

	CT	
	Present	Absent
Histology (+)	6	3
Histology (-)	3	15
	9	18

Table II. Mediastinal lymph node status by CT, analyzed by lymph node level

	CT	
	Present	Absent
Histology (+)	6	4
Histology (-)	4	61
	10	65

different threshold values of SUV were used to diagnose a primary malignant lung tumor as opposed to a mediastinal lymph node metastasis. Because the background uptake of glucose per unit volume in the normal lung is low, we have found that a relatively low radionuclide concentration, corresponding to an SUV of 2.0, differentiates malignant from benign lung masses with a high degree of accuracy. We⁷ therefore consider masses in the lung with an SUV greater than 2.0 to be malignant. The background rate of glucose uptake per unit volume in the mediastinum is normally greater than that in the lung. On the basis of previous, unpublished, data, we have chosen an SUV of 4.2 as the threshold value for differentiating benign from malignant tissue in the mediastinum. Therefore, areas of FDG uptake in the mediastinum with an SUV greater than 4.2 (excluding the heart) were considered to have a rate of glucose metabolism consistent with that of malignant tissue.

The location of specific areas of increased uptake in the mediastinum was assigned by the nuclear medicine physician according to the American Thoracic Society lymph node mapping system. If no specific areas of increased uptake in the mediastinum or supraclavicular regions were identified, the nuclear medicine physician identified the pixel within the mediastinum (noncardiac portion) with the greatest concentration of FDG. The SUV for that region was calculated and represented the maximum amount of uptake for the entire mediastinum; for example, if that SUV was smaller than 4.2, then the mediastinum was considered to be free of lymph node metastases.

Surgical confirmation. Proof of the presence or absence of malignancy in primary tumors was obtained for all patients by one or more of the following techniques: bronchoscopy, transthoracic needle biopsy, thoracoscopy, and thoracotomy. Confirmation of the presence or absence of mediastinal lymph node metastases was obtained in all patients by scalene node biopsy, mediastinoscopy, or thoracotomy. All accessible mediastinal lymph nodes were

Table III. Mediastinal lymph node status by PET, analyzed according to patient

	PET	
	Present	Absent
Histology (+)	9	0
Histology (-)	0	18
	9	18

either removed or sampled. The location of mediastinal lymph nodes was determined by the thoracic surgeon during the operation by means of the American Thoracic Society lymph node map. Biopsy specimens of bulky nodal metastases were assigned to the closest corresponding lymph node level. Lymph nodes from level 10R were considered mediastinal lymph nodes. Both the PET and CT images were available to the surgeon during the operation.

Data analysis. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CT alone and of FDG-PET as an adjunct to CT for the assessment of mediastinal lymph node metastases were determined. Predictions of lymph node status by either method were analyzed by patient, that is, whether a test determined the correct mediastinal node status in a given patient. Mediastinal lymph node assessment by each test was also analyzed by lymph node level. The relative accuracy of CT alone and of FDG-PET as an adjunct to CT was compared by applying the McNemar test for correlated proportions (exact test, one-sided).¹¹ A *p* value of 0.05 or less indicated a statistically significant difference between the two methods.

Results

Patient population. A total of 27 patients underwent both CT and FDG-PET. The group included 5 women and 22 men, with an average age of 64.4 years (range 40 to 85 years). All patients underwent CT followed by FDG-PET. CT and FDG-PET were performed within 9.2 ± 1.6 days (mean $\pm$ standard error of the mean) of each other (range up to 30 days). Three patients underwent both studies on the same day. A total of 19 patients underwent both studies within 8 days or less. All patients had NSCLC. There were 10 adenocarcinomas (including 1 bronchioloalveolar carcinoma), 13 squamous cell carcinomas, 4 large-cell carcinomas, and 1 NSCLC. The primary cancers ranged in size (greatest dimension) from 1.2 to 10.0 cm, with an average size of 3.8 ± 0.4 cm (mean $\pm$ standard error of the mean).

Surgical staging. The study participants underwent the following surgical staging procedures: mediastinoscopy (*n* = 9), thoracotomy (*n* = 19), thoracoscopy (*n* = 1), and scalene lymph node biopsy (*n* = 2). A total of 75 (2.8 per patient) mediastinal

Table IV. Mediastinal lymph node status by PET, analyzed by lymph node level

	PET	
	Present	Absent
Histology (+)	10	0
Histology (-)	1	64
	11	64

(N2 or N3) lymph node stations were sampled. Cancer cells were present in 10 of 75 lymph node stations (13.3%) and nine of 27 patients (33.3%) according to routine light microscopic analysis.

The mean size ($\pm$ standard error of the mean) of primary tumors without histologically proved mediastinal lymph node metastases was 4.10 ± 0.58 cm compared with 3.22 ± 1.66 cm for primary tumors associated with histologically proved mediastinal lymph node metastases ($p = 0.126$, unpaired t test). The percentage of centrally located primary tumors was higher in the group with histologically proved mediastinal metastases (5/9, 56%) than in the group without histologically proved mediastinal metastases (4/18, 22%).

CT. CT identified the primary tumors in all instances. Pleural effusions were present in three patients. In two of three instances, these were small effusions contralateral to the tumor. Thoracentesis was performed in all cases. The pleural fluid was negative for malignant cells by cytologic analysis. Atelectasis extending to the hilum was present in nine of the 27 patients (in 5/9 with mediastinal metastases and 4/18 without mediastinal lymph node metastases). The primary tumor was described as abutting the visceral pleura in 10 of the 27 patients. No patient had chest wall invasion described on CT, and chest wall invasion was not found during the surgical staging procedures. Mediastinal invasion was described in one patient, who had a hard, fixed mass in the same location at the time of mediastinoscopy. No evidence of bone, liver, or adrenal metastases was noted by CT in any patient.

The data were analyzed for patients and by individual lymph node levels. CT incorrectly staged the mediastinum as "positive" or "negative" for lymph node metastases in three patients each. CT correctly predicted the presence or absence of lymph node metastases in 21 of the 27 patients. CT sensitivity and positive predictive value were 67% (6/9), whereas specificity and negative predictive value were 83% (15/18) (Table I). The accuracy of CT was therefore 78% (21/27). None of the patients in

Fig. 1. CT showing enlarged right paratracheal lymph node (white arrow) in a 65-year-old patient with a primary lung cancer of the right middle lobe. Other CT images showed enlarged lymph nodes along the entire right side of the trachea (extranodal or bulky disease, positive CT results).

whom CT falsely indicated the presence of mediastinal metastases had postobstructive atelectasis or atelectasis extending to the hilum on CT.

When analyzed by individual lymph node station, CT incorrectly identified four stations as positive and four stations as negative. CT correctly identified the presence or absence of lymph node metastases in the other 67 lymph node stations that were sampled. The sensitivity and positive predictive value of CT were 60% (6/10) and the specificity and negative predictive value were 94% (61/65) (Table II). The accuracy of CT in this analysis was therefore 89% (67/75). The specificity was high because of the many true negative mediastinal lymph node levels that were present in the study population.

PET. FDG-PET correctly identified all primary tumors as malignant. The SUV (mean $\pm$ standard error of the mean) for the 27 primary lung cancers was 11.82 ± 1.26 . The SUV for primary tumors associated with mediastinal lymph node metastases was 13.94 ± 2.17 compared with 11.19 ± 1.5 for primary tumors not associated with mediastinal lymph node metastases ($p = 0.44$, unpaired t test). Data regarding mediastinal lymph node metastases were analyzed both for the mediastinum as a whole (analyzed per patient) and for each lymph node level that was sampled for biopsy. PET correctly predicted the presence or absence of lymph node metastases in the mediastinum in all patients (Table III). In this series of patients, the sensitivity and specificity of FDG-PET for staging the mediastinum was 100%. FDG-PET was less accurate

Fig. 2. Coronal FDG-PET image from the same patient showing uptake (SUV = 9.96) in the right middle lobe (*lower arrow*) and uptake consistent with metastatic cancer (SUV = 4.59) in the right paratracheal lymph node chain (*upper arrow*). The right paratracheal lymph nodes contained cancer at mediastinoscopy (both PET and CT had true positive results). Uptake at the lower left side of the patient is from the heart.

Fig. 3. CT of the mediastinum from a 68-year-old man with adenocarcinoma of the right upper lobe showing an enlarged pretracheal lymph node (*white arrow*). FDG-PET measured a maximum SUV of 3.32 for the mediastinum (negative FDG-PET result). This lymph node and others removed at thoracotomy were negative for cancer (CT, false positive result; FDG-PET, true negative result).

at identifying metastases and localizing them to specific lymph node levels (Table IV). FDG-PET mislabeled one histologically negative lymph node level as positive in a patient who had other mediastinal metastases present in other lymph node levels that were correctly identified by FDG-PET. The stage of disease in this patient (according to the criteria of the American Joint Commission on Lung Cancer) was not changed by the false positive designation. When analyzed on the basis of lymph node level, the sensitivity of FDG-PET was 100% (10/10), the positive predictive

value was 91% (10/11), the specificity was 98% (64/65), and the negative predictive value was 100% (64/64). The accuracy of FDG-PET for detecting metastases in individual lymph node levels was 99% (74/75).

Comparison of CT and PET. The McNemar test for correlated proportions (exact test version) was used to compare the ability of FDG-PET and CT to identify the presence or absence of lymph node metastases in patients with NSCLC. A one-sided test was performed. When the data were analyzed for patients, there were six discrepancies between CT and FDG-PET over the presence or absence of lymph nodes in the mediastinum as a whole. In each of these instances, FDG-PET was correct and CT was wrong, as compared with the histologic results. The McNemar test indicated that the difference was significant, with a p value of 0.031. When the analysis was repeated for individual lymph node levels, there were nine differences between CT and FDG-PET, and eight of the nine favored FDG-PET. In this case, the difference was also significant, with a p value of 0.039. We therefore conclude that FDG-PET is more accurate than CT in predicting the presence or absence of mediastinal lymph node metastases in patients with NSCLC (Figs. 1 to 3).

Discussion

The clinical use of PET in patients with cancer is based on an observation by Warburg⁴ that the malignant transformation of liver cells was accompanied by a decreased ability to make energy aerobically. Because anaerobic glycolysis produces much

less energy from glucose, high rates of glucose uptake are necessary for the survival of malignant cells. PET can estimate the rate of glucose metabolism in tissue by measuring the uptake of a glucose analog, FDG, by the tissue over time. FDG is a positron-emitting radionuclide that can be detected by PET. Under steady state conditions, FDG is taken up by cells in a competitive fashion with other hexoses. Once inside the cell, FDG is phosphorylated. It cannot be metabolized further and it cannot diffuse out of the cell. The amount that accumulates in tissue over a certain period provides an estimate of the rate of glucose (hexose) uptake by that tissue. The application of FDG-PET to oncology is based on its ability to detect different rates of glucose metabolism in benign and malignant tissues.⁵

Many studies have documented the ability of FDG-PET to differentiate benign from malignant lung masses.^{5-7, 12-14} We^{7,9} and others⁸ have extended these observations to include the detection of mediastinal and scalene lymph node metastases in normal-sized lymph nodes by FDG-PET. Chin and associates¹⁵ have documented the ability of FDG-PET to detect small foci of lung cancer in single lymph nodes. The results of the current study support these observations. FDG-PET was able to accurately identify lymph node metastases with a low false positive rate. FDG uptake by inflammatory cells can produce false positive readings in patients with pneumonias or active fungal infections.¹⁴ Despite the presence in this study of several patients with postobstructive changes and atelectasis extending to the hilum on CT, FDG-PET was accurate at staging the mediastinum in each. Furthermore, FDG-PET was able to detect scalene lymph node metastases in two patients with metastases to scalene lymph nodes that were not detected either clinically or by CT.

We used a semiquantitative approach to analyze the images generated by the FDG-PET study. We believe the use of semiquantitative methods promises to improve the interpretation of FDG-PET images. A threshold SUV of 4.2 accurately differentiated benign from malignant mediastinal lymph nodes in the current study. More data are required to determine the optimal threshold value for the evaluation of the mediastinum. A quantitative approach will eventually allow investigators to retrieve more information from the images than can be retrieved through visual inspection alone.

FDG-PET supplemented by CT was more accurate than CT alone at predicting the presence or absence of lymph node metastases in patients with NSCLC. CT

provides anatomic detail that cannot be provided by PET. However, CT criteria for detecting lymph node metastases rely on lymph node size. Lymph nodes that contain cancer are often not enlarged, and enlarged lymph nodes often do not contain cancer. Therefore, we believe that the two studies are best used concurrently. Wahl and his group⁸ found that the information provided by computer-generated "fusion" images of standard CT and PET images was similar to that obtained from analysis of the separate images.

The current study provides information that may improve the staging and selection for treatment of patients with NSCLC. The most appropriate use of PET technology in the treatment of patients with malignant disease of the thorax will be determined through further research. We found that FDG-PET supplemented by CT is more accurate than CT alone for staging the mediastinum in patients with lung cancer. We and others are conducting studies designed to investigate the ability of FDG-PET to detect clinically unsuspected distant metastases, to detect recurrent cancer, and to assess the response to treatment of malignant tumors of the thorax. These data could be used to compare clinical algorithms incorporating FDG-PET with current treatment approaches through the use of decision analysis. Cost can be included in this type of analysis. By using these methods, we hope to determine the appropriate, cost-effective use of FDG-PET in the diagnosis and treatment of malignant tumors of the thorax.

REFERENCES

1. Little AG, Stitik FP. Clinical staging of patients with non-small cell lung cancer. *Chest* 1990;97:1431-8.
2. Webb WR, Gatsonis C, Zerhouni EA, et al. CT and MR imaging in staging non-small cell bronchogenic carcinoma: report of the Radiologic Diagnostic Oncology Group. *Radiology* 1991;178:705-13.
3. McLoud TC, Bourgouin PM, Greenberg RW, et al. Bronchogenic carcinoma: analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. *Radiology* 1992;182:319-23.
4. Warburg O. On the origin of cancer cells. *Science* 1956;123:309-14.
5. Nolop KB, Rhodes CG, Brudin LH, et al. Glucose utilization in vivo by human pulmonary neoplasms. *Cancer* 1987;60:2682-9.
6. Patz EF, Lowe VL, Hoffman JM, et al. Focal pulmonary abnormalities: evaluation with F-18 fluorodeoxyglucose PET scanning. *Radiology* 1993; 188:487-90.
7. Scott WJ, Schwabe JL, Gupta NC, et al. Positron emission tomography of lung tumors and mediastinal lymph nodes using [18F]fluorodeoxyglucose. *Ann Thorac Surg* 1994;58:698-703.
8. Wahl RL, Quint LE, Greenough RL, Meyer CR, White RI,

- Orringer MB. Staging of mediastinal non-small cell lung cancer with FDG PET, CT, and fusion images: preliminary prospective evaluation. *Radiology* 1994;191:371-7.
9. Scott WJ, Gobar LS, Hauser LG, Sunderland JJ, Dewan NA, Sugimoto JT. Detection of scalene lymph node metastases from lung cancer: positron emission tomography. *Chest* 1995;107:1174-6.
 10. Tisi GM, Friedman PJ, Peters RM, et al. Clinical staging of primary lung cancer. American Thoracic Society node mapping scheme. *Am Rev Respir Dis* 1983;127:344-7.
 11. Rosner B. *Fundamentals of biostatistics*. 3rd ed. Boston: PWS-Kent Publishing Company, 1990:345-8.
 12. Kubota K, Matsuzawa T, Ito M, et al. Differential diagnosis of lung tumor with positron emission tomography: a prospective study. *J Nucl Med* 1990;31:1927-32.
 13. Knopp MV, Strauss LG, Haberdorn U, et al. Positron emission tomography (PET) with F-18-fluorodeoxyglucose in the imaging and staging of bronchogenic carcinoma. *Eur J Nucl Med* 1991;32:623-48.
 14. Dewan NA, Gupta NC, Redepenning LS, Phalen JJ, Frick MP. Diagnostic efficacy of PET-FDG imaging in solitary pulmonary nodules: potential role in evaluation and management. *Chest* 1993;104:997-1002.
 15. Chin R, Ward R, Cappellari JC, Keyes J, Haponik EF. Mediastinal node (N2) involvement by PET-FDG scanning in non-small cell lung carcinoma (NSCLC): pathologic correlation. *Chest* 1994;106:89S.

Discussion

Dr. Valerie W. Rusch (*New York, N.Y.*). PET is a promising new imaging modality in patients with cancer because it can potentially distinguish between benign and malignant tissues by exploiting a known biochemical difference, namely, that malignant cells are characterized by increased glucose metabolism and protein synthesis. Dr. Scott and his colleagues have an established interest in studying the role of PET scanning in patients with lung cancer. This study extends their prior work, which showed that PET has about an 80% specificity in identifying malignant lung tumors.

This study is well designed and suggests that PET is more accurate in detecting mediastinal lymph nodal metastases than is CT. However, it emphasizes that PET, like monoclonal antibody imaging, may not be useful in assessing either small primary tumors or normal-sized lymph nodes that are involved by tumor. The study also emphasizes that the spatial resolution of PET is limited.

On the basis of your experience, Dr. Scott, could you comment on several points pertaining to the clinical usefulness of PET? Specifically, what was the sensitivity, specificity, and accuracy of PET in assessing lymph nodes that were 1 cm or less in size? Have you begun to assess the role of CT/PET fusion imaging (as has been done in monoclonal antibody imaging) to try to improve the spatial resolution of PET? Given the limitations of PET that you have outlined, do you foresee situations in which it would replace mediastinoscopy or mediastinal lymph node dissection in the staging of disease in patients with previously untreated lung cancer? I find it hard to understand how these low-risk surgical procedures, which are the gold standard of lung cancer staging, will be supplanted by noninvasive imaging modalities, including PET scanning. What is the current cost of a

PET scan and of the equipment? Could you comment on the relative value of FDG versus methionine scanning? Finally, do you foresee that the most durable application of this new modality may be to detect extrathoracic disease rather than mediastinal nodal metastases or to evaluate patients for recurrent or persistent tumor after nonsurgical treatment?

Dr. Scott. The spatial resolution of PET scan is limited, and that is why we have tried to use CT scan along with it.

In our study, PET correctly identified four lymph node levels as positive for metastatic disease in four instances in which CT criteria falsely classified them as negative (<1 cm). There were no lymph nodes 1 cm or smaller classified as falsely positive by PET. At the meeting of the American College of Chest Physicians, Dr. Chin, from North Carolina, reported results of several patients who had lymph nodes less than 1 cm in size, all of whom had metastases detected by PET scan. I think PET can work very well.

We do not use CT and PET fusion images. Dr. Wohl, from Michigan, did not find much difference between using CT as a supplement to PET, as we did, and actually trying to fuse the scans into a computer-generated autometabolic image.

I would foresee this modality possibly replacing mediastinoscopy in patients in whom the primary tumor is known to be a cancer and in whom the study shows that there is no uptake in the mediastinum. I think PET is very reliable in that particular instance.

The PET center at Creighton University costs approximately \$2 million. The current cost of PET scans is decreasing all the time. The cost of PET in our study was \$900.

I have not used methionine as a radionuclide. It must be generated on-site because it decays rapidly. It is therefore less practical than FDG. Many people are interested in detecting extrathoracic disease. Those studies are difficult inasmuch as brain metastases cannot be detected very well with this method because of the uptake of FDG by normal brain tissue.

Finally, I think there is a great problem with evaluating recurrent and persistent disease, because inflammatory tissue also takes up glucose. Patients who have radiation treatment and radiation necrosis can have FDG uptake. It is difficult to know whether that represents necrosis or recurrent or persistent tumor.

Dr. William H. Warren (*Chicago, Ill.*). At Presbyterian-St. Luke's Hospital we also have experience with the PET scan. We have studied 24 cases and obtained a false negative result in one. That case, not surprisingly, turned out to be a bronchial carcinoma.

I have one comment regarding your conclusion that the PET scan may supplement the CT scan. In this day of cost containment, given your results and the results of others, I believe PET scans may be more valuable than CT scans and become the study of choice for staging lung cancer.

We have had some difficulty in interpreting the subcarinal nodes because of the uptake in the heart. Have you had this experience and can you give us any help?

Dr. Scott. It is difficult to detect some of the lymph node tissues and tissues in the area of the heart. Our nuclear medicine physician looks for very round areas. We think that illustrates the value of semiquantitative analysis: If we can locate an area like that and the SUV is greater than 4.2, we have had good success in detecting those abnormalities.