GENERAL THORACIC SURGERY

POSITRON EMISSION TOMOGRAPHIC IMAGING WITH FLUORODEOXYGLUCOSE IS EFFICACIOUS IN EVALUATING MALIGNANT PULMONARY DISEASE

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Objective: Positron emission tomography (PET), when used with the intravenously administered radiopharmaceutical F-18 fluorodeoxyglucose (FDG), has the potential to help in the evaluation of patients with lung cancer because the radiopharmaceutical is concentrated by metabolically active cells. We conducted a retrospective study of PET-FDG in 96 patients evaluated at our institution over the past 2 years for suspected primary pulmonary neoplasms. PET-FDG results were compared with the findings of computed tomographic scans on the same patients. All patients underwent surgical exploration with or without resection of the malignant tumors. Sites of potential malignancy were subjected to biopsy and/or excision, with subsequent pathologic evaluation. **Results:** A total of 96 patients with suspected or proven primary pulmonary malignant disease were evaluated. Sixty-six patients had histologically confirmed malignant tumors, and 30 had benign masses histologically. PET-FDG had an accuracy of detecting malignancy in pulmonary lesions of 92% (sensitivity 97%; specificity 89%). A total of 111 surgically sampled sites were from lymph nodes. PET-FDG was accurate in predicting the malignancy of nodes in 91% of instances, whereas computed tomography was correct in 64%. The sensitivity, specificity, and predictive accuracy of PET in detecting metastatic lymphadenopathy in mediastinal lymph nodes were 98%, 94%, and 95%, respectively. PET-FDG also changed the M stage in 8 (12%) patients (6 with and 2 without metastases). The 6 malignant (positive) lesions were correctly identified by PET-FDG, and the 2 without tumor were accurately predicted as benign (negative). **Conclusion:** These initial results suggest that PET-FDG is highly accurate in identifying and staging lung cancer. PET-FDG also appears to be more accurate in detecting metastatic mediastinal lymphadenopathy than computed tomographic scan. (*J Thorac Cardiovasc Surg* 1999;117:719-27)

Precise evaluation of the patient with a suspected primary pulmonary malignant tumor continues to be a problem for thoracic surgeons. Accurate preoperative

assessment of the exact nature of a pulmonary lesion remains challenging. Even more challenging is the determination of whether lymph node involvement and

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distant metastases exist at the time of presentation. Several imaging techniques are currently available that can help in the assessment of primary pulmonary malignant tumors and their potential sites of metastatic extension. Computed tomography (CT) is an established imaging modality that has been used frequently to evaluate pulmonary neoplasms since its inception. Positron emission tomography (PET) is an emerging imaging technique that shows great promise for evaluating malignant pulmonary tumors and their metastases. Like all diagnostic tests, both CT and PET have their assets and liabilities.

CT is readily available and can be obtained in virtually every hospital. As with all imaging techniques, the quality and quantity of information obtained is dependent on the sophistication of the scanning apparatus used. Modern CT equipment yields high-resolution images of the chest in the axial orientation, which provide excellent anatomic definition of intrathoracic structures. Studies that have evaluated the ability of CT to predict involvement of mediastinal lymph nodes in patients with lung cancer have yielded disappointing results, because CT can predict nodal involvement only by enlargement (diameter > 1 cm) or by morphologic abnormality.¹⁻³ Confirmation of nodal involvement by the pulmonary malignancy, therefore, has required mediastinoscopy and pathologic examination of biopsy specimens.^{4,5} The inability of CT scan to recognize metastatic disease in nodes of normal size has been noted by several authors.^{6,7}

PET scans have the ability to detect cancers by use of the intravenously administered radiopharmaceutical F-18 fluorodeoxyglucose (FDG), which is a D-glucose analog that is concentrated by metabolically active cells such as those found in malignant tumors.^{8,9} This technique is limited not only by the activity of the cells present but also by physical volume of tumor, because tumor volumes of less than 1 cm are more difficult to detect due to PET resolution.¹⁰ Inflammatory processes can produce false positive results with PET. Additionally, malignant tissue that is near ventricular myocardium could be difficult to separate from the heart, because metabolically active cardiac myocytes concentrate FDG well.

To assess the efficacy of PET-FDG imaging in patients with suspected primary pulmonary malignant disease, we conducted a retrospective analysis of our patients over a 2-year period. We focused on the ability of PET-FDG to define the nature of the pulmonary lesion, to assess the status of each patient's mediastinal lymph nodes, and to detect distant metastases. In each patient the results of the PET scan were compared with

those of the CT scan. The diagnostic efficacy of each method was compared.

Methods

We reviewed the charts of all patients who were sent to the Mary Babb Randolph Cancer Center of West Virginia University School of Medicine for evaluation and treatment of primary pulmonary malignant disease between October 1995 and October 1997. All patients who had some type of diagnosed or suspected pulmonary malignant disease were included. Those patients who had already started to receive therapy for malignant disease before our initial evaluation were excluded. All patients received a complete history and physical examination. Standard chest radiographs (both posteroanterior and lateral) were obtained on all patients if they had not had such examinations performed within a month of our initial evaluation. If the patients had had a chest CT scan performed at another institution, the scan had to be a high-resolution examination performed with intravenous contrast medium and had to include the neck, thorax, and upper part of the abdomen. If such a CT scan had not been obtained, one was ordered as part of the initial evaluation. These CT scans were performed with GE 9800 systems (GE Medical Systems, Waukesha, Wis). Contrast (Hypaque 60 or Omnipaque 300) consisted of 100 to 200 mL injected intravenously. Complete examinations were obtained both with and without contrast medium. All PET scans were obtained within 1 month of the CT scans.

All PET scans were performed at our institution with a GE Advance Scanner (GE-1995). Informed consent was obtained from all patients. The resolution of this scanner is 4.7 mm in the transverse plane. Its field of view is 14.6 cm. Two distinct scans were obtained: one emission and one transmission scan. In the former, the scanner recorded, stored, and analyzed all the data generated from the positron activity emitted from the injected FDG. PET scans on each patient were performed in 3 to 4 different positions so that the field of view of the scan included all tissues from the neck to the pelvic floor. Emission scans were obtained with an acquisition time of 5 minutes per field of view. Transmission scans were obtained for 10 minutes in each position. The transmission scan causes sequential cuts to be generated from a positron beam, which is directed through the patient to generate attenuation data due to the body's inherent tissue characteristics. This allows the computer in the scanner to correct for background scatter and produce a corrected image. Each patient was given an intravenous injection of 10 mCi of FDG after having received nothing by mouth for at least 4 hours. An emission scan of the patient's body was then obtained 1 hour after the injection of the FDG. A transmission scan was performed directly after the emission scan. The scanner's computer collected all of the data from the patient's emission scan and corrected the images using the transmission attenuation information to obtain clarified images in sequential axial projections. The data were then reexamined by the computer and reformatted in the sagittal and coronal planes such that at

Table I. Histologic results of malignant pulmonary tumors (*n* = 66)

	No. of patients with diagnosis
Adenocarcinoma	35
Large cell	4
Poorly differentiated	1
Mixed pattern	9
Squamous cell carcinoma	10
Small cell carcinoma	2
Various other malignant tumors	5
Breast cancer	1
Neuroendocrine tumor	1
Thymic tumor	1
Lymphoma	2
Total patients	66

least 35 images were created in each of the 3 orientations (sagittal, coronal, and axial). Partial volume correction was not performed. All of these projections were examined by the radiologist and reports were generated for each patient stating the likelihood of malignancy in the pulmonary mass, the mediastinal nodes, and the possibility of distant metastases. PET scan images were considered to be positive for malignancy if there was focal hypermetabolic abnormality with FDG uptake greater than background or mediastinal activity. Quantitative analysis to compute standardized uptake values (SUVs) was used to differentiate benign from malignant lesions in equivocal cases. SUVs were computed by region of interest analysis. SUVs greater than 3 were considered malignant; this figure is similar to SUV values reported by other investigators.⁷ Similar reports were generated for the CT scans. The radiologist reading the CT scans was different from the one interpreting the PET scans. All images were analyzed qualitatively by visual analysis. The reader was not aware of the histologic results or CT findings at the time of scan interpretation. Data from the PET and CT scans were tabulated and compared.

After a complete preoperative work-up, all patients underwent surgical procedures to delineate the extent of their disease and conduct resections whenever possible. If their disease was deemed far advanced such that surgical resection was not feasible, mediastinal nodes and distant sites of presumed metastases were sampled surgically. All tissues were submitted for pathologic examination. The pathology reports were used to assess the accuracy of the predictions made by CT and PET scans.

Statistical method. Confidence intervals for the PET-FDG and CT proportions (see Table III) are based on large-sample symmetric results; that is, the normal approximation was used to establish upper and lower 95% confidence bounds for the various proportions reported.

Results

A total of 96 patients were evaluated and had complete sets of data. The male/female ratio was 68:28.

Table II. Histology of benign pulmonary lesions (*n* = 30)

Histologic type	No.
Localized fibrosis	10
Granuloma	8
Inflammation	7
Others	5
Sarcoidosis	1
Fungal	1
Lymphoid infiltrate	1
Pseudotumor	1
Cyst	1
Total patients	30

Three of the lesions were read as positive for malignancy by PET-FDG.

Table III. Comparison of CT and PET-FDG in assessing true status of mediastinal lymph nodes (*n* = 111)

	PET (95% CI)	CT (95% CI)
Sensitivity	98% (93.5%-100%)	63% (50.5%-68.9%)
Specificity	94% (88.4%-99.5%)	60% (48.8%-72.4%)
Accuracy	95% (91.6%-99.4%)	61% (48.1%-76.1%)
Positive predictive value	91% (83.9-99.5%)	64% (39.5%-85.9%)

All values are expressed with 95% confidence intervals (CI). PET, Positron emission tomography; CT, computed tomography.

Sensitivity = (True positives)/(True positives + False negatives).

Specificity = (True negatives)/(True negatives + False positives).

Accuracy = (True positives + True negatives)/(True positives + True negatives + False positives + False negatives).

Positive predictive value = (True positives)/(True positives + False positives).

The mean age was 65.9 years (range 43-80 years). Of the 96 patients, 66 were found to have true malignant tumors. The remaining 30 had various benign processes causing the masses in their lungs. Of the 96 pulmonary lesions, 43 were smaller than 3 cm and 53 were larger than 3 cm. The pathologic studies of the malignant lesions showed that the vast majority were non-small cell carcinomas (Table I). The largest number of these were adenocarcinomas. All but 2 of the malignant tumors were detected and correctly predicted by PET-FDG. The 2 that were missed were both small bronchoalveolar cell carcinomas (1-2 cm), which were included in the total adenocarcinoma group. In reviewing the histologic slides after realizing that these were both false negative tumors, we determined that the lesions were very well differentiated and showed few indications (eg, few mitotic figures per high-power field) of increased metabolic activity.

Most of the benign lesions showed histologic patterns consistent with healing inflammatory processes

Fig 1. A PET-FDG imaging study (coronal view) demonstrating intense FDG uptake in the hilar area of the right lung in a patient with a primary lung cancer. There are also focal areas of enhanced uptake consistent with metastatic lymph nodes in the right infrahilar and left perihilar regions.

(Table II). The granulomas that were encountered showed a wide range of inflammation and healing. Some were quite organized and showed dense scarring. Others appeared to be more active and possessed areas of acute inflammation. Three of these were interpreted by PET-FDG scans as being malignant (3 false positives). Since we culture our specimens routinely, the culture results on these were obtained. Two showed no growth even on prolonged selective cultures. One, however, did grow *Cryptococcus neoformans* organisms on definitive cultures. SUVs in inflammatory false positive lesions were less than 5 and so were classified as mild to moderate.

A total of 111 mediastinal lymph node stations (from 44 patients) were evaluated by PET-FDG and CT scans. Pathologic examination showed that 45 stations had malignant infiltration and 66 were benign. Only 8 lymph nodes were larger than 3 cm; the others were smaller than 3 cm. After the pathology reports were correlated with CT and PET-FDG data, the accuracy, sensitivity, specificity, and predictive values for both modalities were calculated (Table III). In 26 stations in which CT scan predicted that lymph nodes that were enlarged (>1 cm) would be malignant, PET-FDG correctly predicted that the nodes would be benign. Similarly, in 15 lymph node stations that were predicted to be benign by CT (<1 cm), PET-FDG accurately

predicted that they would contain metastases. Five of 16 nodal stations missed on CT showed N3 disease. All told, PET-FDG changed preoperative staging for N in 31 (for a total of 41 stations) of 66 patients (47%).

PET-FDG proved very capable of identifying unsuspected distant metastases and of determining the true nature of suspected metastases. In 6 patients true distant metastases were confirmed when none was suspected. In 4 patients bony metastases were identified. The presence of bony metastases was confirmed on biopsy ($n = 1$) or magnetic resonance imaging findings ($n = 3$). In the remaining 2 patients, 1 adrenal mass and 1 cervical lymph node were identified as true distant metastases. The adrenal mass was confirmed as a metastasis by needle biopsy. Excision of the cervical lymph node with subsequent pathologic examination confirmed metastasis. In 2 other instances, lesions that were suspected to be metastases were read by PET-FDG as having no metastatic tumor activity. The adrenal mass was subjected to subsequent needle biopsy and was found on pathologic examination to be an adenoma. The other suspected bony metastasis was detected initially by a bone scan but was read as benign by PET-FDG. The patient underwent resection of the primary tumor and has subsequently undergone several bone scans, all of which showed no suspicious activity in the lesion previously thought to be a metastasis on the basis of the initial bone scan.

Discussion

PET-FDG scan was very capable in our experience of detecting true primary pulmonary malignant tumors. Others have had similar results in evaluating primary pulmonary malignant lesions with PET-FDG. Kubota and associates¹⁰ studied 22 patients with noncalcifying lung tumors and found that PET-FDG had a sensitivity of 83%, a specificity of 90%, and an accuracy of predicting malignancy of 86%. Valk and associates⁶ studied 102 primary lung cancers in 99 patients and found that better localization of primary lung tumors was achieved when both transmission and emission scans were used in conjunction. These authors, however, did not report numbers on the accuracy of PET-FDG in predicting the malignancy of suspected primary pulmonary neoplasms. Scott and associates¹¹ reported on 62 patients with lung tumors evaluated by PET-FDG. The sensitivity and specificity of PET-FDG imaging for differentiating benign from malignant primary lung tumors were 93.6% and 80%, respectively. Accuracy in this same study was 90%. The positive and negative predictive values were 93.6% and 80%, respectively. Hence PET-FDG can be expected to be approximately

Fig 2. The plates presented in this figure demonstrate the utility of collecting PET images in multiple projections. **A**, A selected cut from a chest CT scan taken in a 62-year-old woman who had a primary pulmonary malignant tumor at the hilum of the left lung. **B**, A selected coronal image in the same patient shows a prominent left hilar carcinoma just above the area of intensity generated by the ventricular myocardium. A metastatic nodule is apparent in the right paratracheal region near the head of the clavicle. The area of intense activity low in the projection represents residual metabolized FDG present in the patient's urinary bladder. **C**, This parasagittal view in the same patient shows part of the metabolic activity recorded from PET-FDG in the heart and bladder, as well as the metastatic nodes in the superior mediastinum. Most important, it detected a metastatic bone lesion that was a previously unsuspected metastasis in the spine, seen at the *far right* of the image.

90% accurate in detecting the true malignant nature of a primary pulmonary neoplasm.

The problem of false negative results on PET-FDG still exists, because the scanner has a finite lower limit of spatial resolution and is dependent on the level of metabolic activity inherent in the tumor cells.^{8,10} The sophistication of the scanning apparatus we used allows theoretic detection of tumors to 4.7 mm in great-

est diameter. This is better resolution than that reported for earlier units, which had a theoretic lower limit of 1 cm.¹⁰ There were still 2 false negative results, however, and these were in small nodules that had relatively quiescent malignant neoplasms. Differentiation of true malignant neoplasms is more difficult for PET-FDG when the metabolic activity of the neoplasm is low.¹² Of all lung cancers, bronchioloalveolar cell carcinoma

appears to be the most likely to cause false negative readings on PET-FDG because of its relatively low metabolic activity.¹¹ In one study, 3 false negative readings on PET-FDG were obtained: 2 were on tumor masses smaller than 1 cm in diameter and the third was on a bronchioloalveolar carcinoma.¹¹ One recent study by Kim and colleagues¹³ has even suggested that peak SUVs should be used in evaluating all malignant pulmonary lesions. In their study conducted on 48 patients, they found that the mean peak SUV for bronchioloalveolar carcinoma was significantly less than those values recorded for squamous cell carcinoma and for adenocarcinoma.¹³ Unfortunately, those authors did not include any data on peak SUVs on patients who had granulomatous lesions in their lungs. Such a comparison would be helpful inasmuch as the SUVs on PET-FDG may well be comparable with those seen for relatively low-grade carcinomas.

In our study PET-FDG read 3 benign lesions as malignant. These false positive results were all due to granulomatous inflammatory processes. As noted previously, acute and indolent processes can concentrate PET-FDG due to the increased metabolic activity seen in the inflammatory cells.¹⁴ This may occur since FDG is known to accumulate in macrophages in granulation tissue that may surround an inflammatory or a neoplastic process.^{15,16} Others have noted that histoplasmosis and related organisms are particularly prone to causing false positive PET-FDG readings.¹¹ Hypermetabolism has been described in both inflammatory and granulomatous lesions to a degree that will cause false positive PET-FDG determinations in aspergillosis and active tuberculosis as well.^{17,18}

One recent study addressed the relative mean SUVs between benign and malignant pulmonary lesions.¹⁹ In this study 59 patients with cancer had a significantly higher mean standardized uptake ratio than 28 patients with benign disease. (8.01 ± 6.09 for malignant vs 2.99 ± 0.49 for benign). Most notably, these same authors showed that in their series PET-FDG was able to identify correctly all intrathoracic recurrences in the patients they studied with primary pulmonary malignant tumors.

The superiority of PET-FDG over CT in determining the correct status of mediastinal lymph nodes in patients who have primary pulmonary malignant disease is well established. Several authors have published data that support our findings.^{6,7,11,20} Valk and associates⁶ found that the sensitivity and specificity for PET-FDG in detecting N2 disease were 83% and 94%, respectively, whereas the comparable figures for CT were 63% and 73%, respectively. Steinert and col-

leagues⁷ found that the sensitivity of PET and CT was 89% and 57%, respectively, for the staging of N2 or N3 disease in mediastinal nodes. These same authors found that specificity for N2 and N3 disease was 99% for PET and 94% for CT, and the positive predictive values for these 2 imaging modalities were 96% and 76%, respectively. Scott and colleagues¹¹ believed that PET-FDG was a highly accurate noninvasive method for identifying malignant lung tumors but had to have the data from prospective studies before its value in assessing N2 disease could be determined. Vansteenkiste and associates²⁰ believed that the results of PET-FDG were superior when they were used in conjunction with CT data. Currently, most investigators think that PET-FDG is superior to CT but that the two should be used together to achieve the highest possible accuracy in assessing the status of mediastinal lymph nodes.²⁰ After collating the CT and PET data presented herein, we also found that the accuracy of the two techniques improves when the information from CT and PET are considered in concert.

We found PET-FDG quite helpful in detecting unknown metastatic sites. Other institutions have had similar experiences.^{6,21,22} Using PET-FDG, Valk and colleagues⁶ found 11 (11%) patients with previously unsuspected distant metastasis, with no demonstrated false positive results. One recent report stated that PET had an accuracy of 96% in the detection of M stage in patients with primary pulmonary malignant tumors.²¹ Detection of unsuspected cancer in scalene lymph nodes has been reported by others.²² In all, we believe that PET-FDG has a large potential for detecting unsuspected metastatic lesions caused by primary pulmonary malignant tumors. More data need to be available before firm guidelines can be established. In our study helical CT scanning was not performed. It is possible that use of helical CT may improve sensitivity.

One place wherein PET-FDG may be less useful in detecting metastases is the perinephric tissues, because FDG is concentrated by the kidneys and excreted in the urine. In our own experience we have found it difficult to distinguish metastatic implants from renal parenchyma. As reported in this work, we think that PET-FDG is quite capable of determining the true nature of masses found in the adrenals in patients with primary pulmonary malignant tumors. Others share this opinion.²³ In a study that evaluated the ability of PET-FDG to determine the true nature of masses in patients with cancer, 24 adrenal masses were evaluated in 20 patients.²³ The authors concluded that PET-FDG helped determine the correct differentiation between benign and malignant lesions in the adrenals.²³

Certainly more data are needed for patients with primary pulmonary malignant disease, but the initial data suggest that PET-FDG may be very helpful in determining the true nature of potential adrenal metastases.

In summary, PET-FDG has a high degree of sensitivity, specificity, and accuracy in denoting the true nature of a pulmonary mass. PET appears to be superior in delineating the true involvement of mediastinal lymph nodes by primary pulmonary malignant disease. PET is also very capable of identifying the presence of occult metastases. False positive results may be obtained by PET from lesions that have a high degree of metabolic activity, such as active granulomatous lesions. False negative PET results may occasionally occur in patients who have malignant tumors with cells that are less metabolically active. In all, we believe that PET scanning is an important tool in evaluating patients with suspected lung cancer, because it gives important information that allows more accurate preoperative staging and could result in improved patient management.

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Discussion

Dr Joel D. Cooper (*St Louis, Mo*). Dr Graeber, I want to congratulate you and your coauthors for a very important paper.

Years ago when I was in Toronto at the dawn of the magnetic resonance imaging era, we evaluated magnetic resonance imaging for lung cancer in the hopes that it would reflect not just the size of lymph nodes but perhaps their content. We used to refer to it as a "magnetic biopsy." However, it was of no additional value to CT in the staging of lung cancer because it detected physical presence, not content. Thus it was with some skepticism that we viewed the advent of PET with its proposed ability to do a metabolic biopsy.

Our experience to date, mainly with esophageal cancer and more recently with lung cancer, has turned our skepticism into enthusiasm. We previously reported, for esophageal cancer, exactly the same type of experience that you have reported with lung cancer. In about 100 consecutive cases of

esophageal cancer, only 2 tiny 1- to 2-mm mucosal lesions were undetected. All other primary sites were detected.

As in your report, metastases, unsuspected on the basis of CT scan, were detected and proven by biopsy. Also as in your report, staging was changed in about 25% of cases by the addition of PET to the other standard techniques for staging. Our experience with the use of PET scanning for lung cancer has been less focused and less rigorous, perhaps because we have just begun to gain experience. However, I share your enthusiasm for it. As a long-time proponent of mediastinoscopy before thoracotomy for all patients with lung cancer, I believe the day will come when a combination of a negative PET and a negative CT will preclude the need for doing mediastinoscopy.

I would like to share a couple of caveats to emphasize points you made and ask a few questions. As you have demonstrated, the image in the PET scan relates not to the physical size of the lesion but to its intensity. A bright image may be large, but it has nothing to do with the actual size of the lesion. Because of this, it will eclipse any surrounding or adjacent lymph nodes, which cannot be detected. Thus adjacent nodes cannot be seen in esophageal cancer, and I would propose that for hilar lesions of the lung, adjacent lymph nodes probably would not be seen. Is this also your impression?

Second, there is no clear-cut definition of what constitutes a positive PET scan. We find that the assessment is observer-dependent, depending on the experience of the observer. Do you find that to be true as well? False negatives at the primary site with lung cancer in our experience have occurred in exactly the circumstances you have mentioned, namely, slow growing bronchioloalveolar carcinomas with a low metabolic rate.

Have your results in this study yet changed your approach to the use of mediastinoscopy for the diagnosis of metastatic nodes? Is the PET scan in your institution read in conjunction with the CT scan? If so, this does not replace the CT scan, and I believe your manuscript makes that point quite clearly.

Finally, you found 4 bony metastatic lesions. Was biopsy or clinical follow-up used to confirm these findings?

Dr Graeber. Thank you, Dr Cooper. I think it is evident from Dr Cooper's comments and from mine that we are still in the middle of the learning curve regarding use of PET. It is difficult to define masses that are close together, and indeed we have had difficulty in defining masses that may be very close to the active myocardium. We have also had difficulty in finding masses that are present within the renal parenchyma, because the dye is concentrated in this area.

The PET scan is dependent on the observer and on an evaluation process. Articles are being presented which suggest that the SUVs, which take the actual counts and then take out the background information, are now being taken from lesions and being compared. One article in the *Journal of Radiology* compared SUVs and found a statistically significant difference between benign lesions, such as granulomas that we found, and bronchoalveolar cell carcinomas. We are starting to use the SUVs.

We have changed our approach to mediastinoscopy somewhat, but we still need more information, and we have started on a prospective study to get that information.

We do use both the CT scan and the PET scan together. We gain more information from using both, and we do not believe in disregarding good information. Others have just started to report this in the radiologic literature and have shown increased accuracy by using both scans versus using each individually with separate radiographers reading the scans. Also, we did confirm our bone biopsies in all but one instance. The other instance was confirmed by serial bone scans, which showed negativity, and that was in the benign lesion.

Dr Michael A. Grosso (*Browns Mills, NJ*). We were just referred a patient who had a negative PET scan, with a 1.5-cm lesion in the right upper lobe. She was counseled by her pulmonologist not to undergo any invasive testing but to wait another 6 months or longer and have the scan repeated. She was uncomfortable with this advice. We resected the lesion, and it was an adenocarcinoma of the lung.

I wish to inject a note of caution, not so much about the fallibility of the scan, but about some of the advice that may be given to patients on the basis of the results of the scans.

Dr Graeber. I agree with your caution. I have had similar experiences. We are not yet at a point where we can make those determinations. If the scan results were negative in one of my patients, I, too, would obtain a biopsy of the lesion and send it to a pathologist.

Commentary

The current study by Graeber and associates provides further compelling support for the use of FDG-PET imaging in diagnosing and staging lung cancer. These investigators, like others, have elucidated the limited role of conventional anatomic imaging, which describes the location and morphologic characteristics of primary lung lesions, as opposed to PET, which provides metabolic information, in evaluating patients with possible lung cancer. PET helps to differentiate benign from malignant abnormalities indeterminate by CT. In fact, the authors of this study found PET to be 92% accurate in making this distinction. The implication for patients with an indeterminate pulmonary abnormality is not trivial. In some series, up to 50% of these abnormalities are proved to be benign after surgical resection. A negative PET obviates the need for this unnecessary intervention in many cases.

Similarly, hilar and mediastinal lymph node size and morphology as assessed by CT is clearly a suboptimal staging procedure with sensitivities and specificities about 60%. In the current and prior studies, PET was significantly more accurate than CT (91% vs 64%) as a predictor of nodal disease. Ideally, further investigations will elucidate which surgical patients can go

directly to primary resection and which patients will require lymph node sampling.

In describing other findings on the staging PET study, the authors found 12% of patients had a change in their M stage as compared with conventional imaging. This resulted in more accurate overall staging and thus more appropriate patient treatment.

Although this and other series have demonstrated the clinical utility of FDG-PET in complementing conventional studies, perhaps more important is the entirely new direction PET has taken diagnostic radiology.

It is a model system for molecular imaging, and as more is understood about basic tumor biology, we will be able to incorporate metabolic, biochemical, or even genetic changes of tumors in the effort to develop a noninvasive tumor profile. These tumor characteristics detailed by imaging should provide essential diagnostic information with prognostic and therapeutic implications.

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