FDG SPECT in Patients With Lung Masses*

Suzanne T. Mastin, MD; Walter E. Drane, MD; Eloise M. Harman, MD, FCCP; James J. Fenton, MD; and Larry Quesenberry, MSN, RN, CCRN

Study objectives: To determine whether 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG) single-photon emission CT (SPECT) is useful in characterizing pulmonary masses.

Design: Scans were prospectively acquired and interpreted. Interpretations were performed with CT or chest radiograph but interpreters were blinded to eventual diagnosis.

Setting: University hospital practice and affiliated Veterans Administration medical center.

Patients or participants: Forty patients participated as part of an institutional review board-approved research protocol, and informed consent was obtained in all. Eight additional patient scans were acquired as part of their clinical evaluation for pulmonary mass.

Measurements and results: There were 26 malignant lesions (12 were 1 to 2 cm in size, the rest were larger) and 17 benign lesions (3 were <1 cm in size, 9 were 1 to 2 cm in size, and 5 were larger). Averaged sensitivity, specificity, positive predictive value, and negative predictive value were, respectively, 50% (12 of 24), 94% (17 of 18), 92% (12 of 13), and 59% (17 of 29) for lesions 1 to 2 cm in size, 100% (28 of 28), 90% (9 of 10), 97% (28 of 29), and 100% (9 of 9) for lesions >2 cm in size. There was good correlation between readers (p < 0.0001).

Conclusion: FDG SPECT is useful in characterizing pulmonary masses >2 cm in size and appears to be equivalent to positron emission tomography for these lesions. Although currently clinically suboptimal for characterizing lesions ≤2 cm in size, FDG SPECT appears to be better than current anatomic imaging methods. In addition, the positive predictive value of FDG SPECT for small lesions is also high (92%), and this technique appears potentially useful in the subset of patients in whom a positive result would alter clinical diagnostic pathways or care.

Key words: emission CT; lung neoplasms; lung nodule; radionuclide studies

Abbreviations: CXR = chest radiograph; FDG = 2-[fluorine-18]fluoro-2-deoxy-D-glucose; FWHM = full-width-half-maximum; PET = positron emission tomography; SPECT = single-photon emission CT

Cancer statisticians estimate 171,500 new lung cancers would be detected in 1998.1 Because only one third of malignancies present as nodules, and 35% of nodules found on chest radiographs (CXR) are malignant, it could be estimated2 that approximately 152,000 new pulmonary nodules would be found in 1998. Conventional imaging techniques are able to differentiate benign from malignant pulmonary nodules in only a small percentage of cases before biopsy or other interventional procedures.3,4 An accurate, cost-effective, accessible method to noninvasively determine whether a pulmonary nodule is benign or malignant could decrease patient morbidity and health-care resources and dollars now devoted to evaluation of pulmonary lesions.

The literature has shown that 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG) uptake in a solitary pulmonary nodule determined by positron emission tomography (PET) imaging demonstrates malignancy with a high degree of accuracy.5-9 but PET scanners are not accessible to a large number of patients. Single-photon emission CT (SPECT) imaging of FDG is feasible,10 is relatively inexpensive, and has been validated by several authors for imaging viable myocardium.11,12 Although the resolution of FDG SPECT does not approach that of PET equipment at this time and use of FDG SPECT for tumor imaging is controversial,13,14 SPECT equip-
ment adapted for high-energy imaging offers many practical solutions to some of the prohibitive aspects of clinical PET.

We undertook a prospective investigation of FDG SPECT in patients with lung masses to determine preliminary sensitivity and specificity of the technique.

**Materials and Methods**

Forty-eight patients with pulmonary masses were evaluated prospectively from February 1994 to December 1997. Patients with indeterminate masses—on CXR or CT—were recruited. Initially patients with large masses were included in the study; once adequate imaging results were established, emphasis switched to lesions \( \leq 4 \text{ cm} \) in size. Forty studies were performed as a research investigation approved by the institutional review board of our health science center, and informed consent was obtained from all 40 patients. In these patients, clinicians were blinded to the results of the FDG study, and imaging results had no impact on clinical care. Eight studies were performed as clinical cases, and imaging results were used in combination with results of other tests in determining appropriate care.

Patients reported with a minimum of 4-h fast except in three patients: two with diabetes who ate a light lunch or snack approximately 1 to 2 h before injection and one patient who did not disclose mild hearing impairment at the time of recruitment and did not comply with instructions given over the telephone. After informed consent, doses of 185 to 444 MBq (5 to 12 mCi) were given IV and SPECT imaging was performed after a 45- to 120-min delay. FDG was prepared at a remote site the morning of the exam and shipped by courier to our hospital, which is 2 h away. This imposed some restrictions in the times that scans could be performed, and variability in imaging time after injection occurred in some patients because of conflicting clinic appointments or tracer delivery problems.

Scans were performed with a two-headed camera with high-energy collimation (17 mm full-width-half-maximum [FWHM] at 11 cm depth). Two to three sequential 12-min scans were performed in each patient. Scans were acquired in step-and-shoot mode with 60 stops at 6° intervals with 10 s of data acquisition at each stop. Images were acquired into a shoot mode with 60 stops at 6° intervals with 10 s of data performed in each patient. Scans were acquired in step-and-shot appointments or tracer delivery problems.

Interpretative results are provided by size in Table 2. Representative studies are presented in Figures 2 and 3.

**Results**

Of the 43 patients with adequate lesion characterization, there were 26 biopsy-proven primary lung malignancies and 12 biopsy-proven benign processes (Table 1). Five abnormalities were characterized with CT or MRI. Two abnormalities were stable for \( \geq 2 \) years, one abnormality disappeared on follow-up CT, one “lesion” was clarified as a pulmonary vein, and one “lesion” was demonstrated to be a pleural plaque. FDG SPECT results are given for all lesions in Table 2. Representative studies are presented in Figures 2 and 3.

There were five congruent false-negative interpretations. All lesions were \( < 2 \) cm in size. One false-negative interpretation occurred in a patient with diabetes who had a light lunch 2 h before FDG administration. There were two lesions that were 1.5 cm in maximal diameter and did not take up FDG. These lesions were characterized as false-negatives but the scans were interpreted as positive because of prominent uptake within mediastinal lymph nodes (Fig 4). In addition there were two false-negative interpretations by reader 1; both lesions were \( \leq 2 \) cm in size, and low-grade activity was called positive by the second reader in these cases.

**Discussion**

FDG for tumor detection has been one of the most promising areas of imaging research in the past
two decades. FDG imaging affords unique and valuable metabolic information about glucose utilization in malignant masses and has been helpful for detecting a wide variety of primary lesions. One of the strongest areas of FDG use is pulmonary lesion characterization using PET imaging with sensitivity of 93%, specificity of 88%, and accuracy of 92% in one recent study of radiographically indeterminate nodules.

Establishing and maintaining a PET center is a very expensive endeavor, and PET centers in our state have decreased substantially in number in the last several years. Patient access is limited and costs of clinical PET are high at a time when fiscal constraints on health-care dollars are very tight. Either SPECT or hybrid coincidence-gamma camera imaging of FDG have the advantages of practicality, economy, and accessibility. These cameras can be maintained in a medium to large nuclear medicine department and used for routine nuclear medicine studies as well as high-energy imaging and can be run by the same technicians who provide routine clinical service. Currently the resolution of FDG SPECT is lower than that of PET, and the sensitivity for detection of small lesions, although controversial, is thought to be comparatively low.

In this study, overall sensitivity, specificity, positive predictive value, and negative predictive value for FDG SPECT were 77%, 91%, 93%, and 72%, respectively. Although these values are less than ideal, they are better than the overall sensitivity of CT or MRI, which are currently used to characterize and stage lesions. Low values are primarily related to the low sensitivity of FDG SPECT for characterization of lesions < 2 cm in size.

Small pulmonary lesions represent a diagnostic challenge for all noninvasive imaging modalities. In this study, sensitivity in patients with lesions 1 to 2 cm was assessed.

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### Table 1—Benign Biopsy Results

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
<td>Hamartoma</td>
<td>2</td>
</tr>
<tr>
<td>Adenoma</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid nodule</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
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<tr>
<td>Hypersensitivity pneumonitis</td>
<td></td>
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<tr>
<td>Fibrosis</td>
<td></td>
</tr>
<tr>
<td>Granuloma</td>
<td></td>
</tr>
<tr>
<td><em>Dirofilaria immitis</em></td>
<td></td>
</tr>
<tr>
<td>Acute and chronic inflammation</td>
<td></td>
</tr>
<tr>
<td>No tumor seen</td>
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</table>

### Table 2—FDG SPECT Results in Benign (n = 17) and Malignant (n = 26) Processes

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
<th>Total</th>
<th>Averages</th>
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</thead>
<tbody>
<tr>
<td>True-positives</td>
<td>19</td>
<td>21</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>True-negatives</td>
<td>16</td>
<td>15</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>False-positives</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>False-negatives</td>
<td>7</td>
<td>5</td>
<td>12</td>
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<tr>
<td>Sensitivity, %</td>
<td>73</td>
<td>81</td>
<td>77</td>
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</tr>
<tr>
<td>Specificity, %</td>
<td>94</td>
<td>88</td>
<td>91</td>
<td></td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>95</td>
<td>91</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>70</td>
<td>75</td>
<td>72</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Histogram of the sizes of benign and malignant masses of ≥ 2 cm.
cm in size (50%) was disappointing (Table 3) but was not unexpected. We found that small malignant lesions have an apparently low uptake on FDG SPECT that approximates background activity, and very close correlation with cross-sectional imaging was required to evaluate these masses. Comparing interpretive results demonstrates that reader 1 read with higher specificity and reader 2 with higher sensitivity. Our interobserver agreement was high at 88% (p < 0.0001). It is possible that FDG SPECT results in small lesion characterization could be improved using fusion imaging, which combines metabolic and anatomic information.

Positive predictive values for 1- to 2-cm lesions with SPECT are high (92%), suggesting that FDG SPECT might be helpful in patients with 1- to 2-cm lesions in whom a positive test might alter management (e.g., confirm malignancy in patients who are not surgical candidates before radiation therapy or hasten surgical treatment vs conservative follow-up).

Additionally, there were two patient studies demonstrating negative uptake in 1.5-cm lesions with avid accumulation in mediastinal lymphadenopathy. Interpretations were classified as false-negatives because of the lack of uptake in the primary lesions; however, the scans were interpreted as positive because of the prominent uptake in the mediastinum. From a patient-management standpoint, the sensitivity of FDG SPECT for lesions 1 to 2 cm in size would be higher at 64%.

Our results for lesions > 2 cm (n = 19) in size are very high—sensitivity 100%, specificity 90%, positive predictive value 97%, and negative predictive value 100%—despite the fact that studies were performed with a 10-year-old camera and relatively low resolution of 17 mm FWHM at 11 cm depth. Our results (Table 1) are equivalent to PET data for lesions of this size,19 and similar findings for FDG SPECT have been reported by Worsley et al21 and Burt et al23 in a direct comparison of FDG SPECT and PET for pulmonary nodules. Taken together, there is good preliminary evidence that FDG SPECT could be a valuable diagnostic test that would add much to conventional imaging evaluation for patients with lesions > 2 cm.
Conclusions

In summary, despite using 10-year-old technology, FDG SPECT appears to be equivalent to PET for characterizing pulmonary lesions > 2 cm in maximum diameter and is more accessible and cost-effective than FDG PET for the large number of patients with lesions of this size. Although currently less-than-ideal clinically for characterizing lesions < 2 cm in size, FDG SPECT appears to be better than CT or MRI for characterizing pulmonary lesions, with a high positive predictive value of 92%. It is possible that with more equipment refinement, our sensitivity for small lesions will approach that of PET, as has been found by Burt et al.23

A major effort in nuclear medicine at present is the development and validation of hybrid coincidence-gamma cameras, not FDG SPECT. At face value, the coincidence approach has much to offer. It has spatial resolution theoretically equal to PET at 5 to 6 mm FWHM. However, this approach is limited by dead-time issues that ultimately cap the achievable count rate and by a critical need for attenuation correction, which is not needed by SPECT. Our data would indicate a strong potential for FDG SPECT and the need for further improvements. We expect that even without improvements in 511-keV SPECT imaging technique, fusion imaging technique might improve the sensitivity of FDG-SPECT for characterization of small lesions.24 In addition, we hope that future developments with the use of thicker crystals to improve sensitivity, better collimators, scatter correction, and depth-dependent resolution recovery will lead to improved spatial resolution of 5 to 9 mm and improved sensitivity so that the unique information provided by FDG imaging will be available to most patients at a reasonable cost.

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