



Positron emission tomography in the diagnosis and staging of lung cancer: a systematic, quantitative review

Barbara MB Fischer, Jann Mortensen, and Liselotte Højgaard

Lung cancer is the cause of 32% of all male cancer deaths and 25% of all female cancer deaths. Because the prognosis depends on early diagnosis and staging, continuous evaluation of the diagnostic tools available is important. The aim of this study was to assess the diagnostic value of dedicated positron emission tomography (PET) and gamma-camera PET in the diagnostic investigation of non-small-cell lung cancer (NSCLC). A systematic literature search was carried out in the MEDLINE and EMBASE databases and the Cochrane Controlled Trials Register. We identified 55 original works on the diagnostic performance of PET with fluorodeoxyglucose in the investigation of NSCLC. For diagnosis of NSCLC, the mean sensitivities and specificities were, respectively, 0.96 (SE 0.01) and 0.78 (0.03) for dedicated PET, and 0.92 (0.04) and 0.86 (0.04) for gamma-camera PET. In the mediastinal staging of NSCLC, the results were 0.83 (0.02) and 0.96 (0.01) for dedicated PET and 0.81 (0.04) and 0.95 (0.02) for gamma-camera PET. We conclude that dedicated PET could be a valuable tool in the diagnosis and staging of NSCLC. However, studies of populations with a lower prevalence of NSCLC are recommended.

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Lung cancer is one of the most common cancers, causing 32% of all male cancer deaths and 25% of all female cancer deaths in the USA.¹ In Denmark, the total annual incidence of cancer is about 320 per 100 000, with 25% of cases being lung cancer. The incidence is falling in men, but it is increasing in women, and Skuladóttir and colleagues have estimated that the classic sex ratio will be reversed in about 15 years.² Lung cancer is now the third most frequent cancer in women in Denmark, and it is causing more deaths among women in the USA than breast cancer.³

Diagnostic procedures and treatments vary from one country to another, as do survival estimates. Overall 5-year survival for patients with lung cancer in Denmark is 5%. For American patients it is 14%.⁴

Smoking is the main cause, leading to more than 90% of lung cancers.¹ Even if everyone stopped smoking tomorrow, the excess mortality among former smokers would take 10 years to fall by half. Consequently, to reduce the incidence of lung cancer, prevention of smoking is important, but not enough. Preventive initiatives should be followed by effective treatment. Early and exact diagnosis and staging are therefore essential.



Figure 1. The picture shows the PET scan of a 66-year-old man. CT showed a 20 mm single pulmonary nodule located anteromedially in the right lung. FDG-PET was positive and the patient was referred to thoracotomy. The tumour was a bronchoalveolar carcinoma.

If lung cancer is discovered at an early, resectable stage, the prognosis is good; 5-year survival after surgery is more than 50% for a stage I cancer.¹ Computed tomography (CT), which can detect tumours as small as 2–5 mm, has an important role in the diagnosis and staging of lung cancer. Positron emission tomography (PET) of fluorine-18-labelled fluorodeoxyglucose (FDG) provides valuable information about the glucose metabolism of tumours larger than 7 mm; high FDG metabolism indicates malignant disease, and low FDG metabolism suggests benign pulmonary changes (Figure 1).

At present, the best PET scanner has a spatial resolution of about 4 mm. In comparison, the resolution of the first

BMBF is a medical student, JM is a consultant, and LH is Head of the PET-unit, Department of Clinical Physiology and Nuclear Medicine, Centre of Diagnostic Investigations, Rigshospitalet, Copenhagen, Denmark.

Correspondence: Dr J Mortensen, Department of Clinical Physiology and Nuclear Medicine, Centre of Diagnostic Investigations, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark. Tel: +45 35 45 40 11. Fax: +45 35 45 40 15. Email: jannmort@rh.dk

Search strategy and selection criteria

This study was initiated in June 1999 with a comprehensive computer search through the MEDLINE and EMBASE databases (Silverplatter, WinSPIRS 4.0) of the medical literature published after 1993. The search strategy was a combination of free text (PET and lung and cancer) and systematic search terms from Thesaurus (tomography-emission-computed; emission-tomography and lung-neoplasm; carcinoma-non-small-cell lung; carcinoma-small-cell; lung-cancer). To avoid missing relevant literature, the search was made as broad as possible by use of the explode function and application of all subheadings to the search terms. The Cochrane Controlled Trials register was also searched for relevant studies. In June 2000, the search was repeated with the help of the Danish Medical Library to identify missing relevant or new studies.

In defining a search strategy, bias will inevitably be introduced into the retrieved material. The most common are publication, language, database, and multiple publication bias.¹⁰ We made no attempt to retrieve unpublished work. This decision was based on the

assumption that most work of reasonable quality on this subject would be published, whether or not the results were significant. A more important bias is language. Egger and colleagues¹⁰ have shown that studies with significant results are more likely to be published in English, whereas those with non-significant results tend to be published in another language. To minimise this bias in our review, we included literature published in German and French.

The most important databases for medical literature are EMBASE and MEDLINE, which cover more than 3000 journals. Both databases were searched, because the estimated overlap in journals is only about 34%, depending on the topic.¹¹

To avoid multiple publication bias, no abstracts or preliminary results followed by later publications were included in this review. However, this approach does not totally eliminate the risk of this bias, because some of the included studies might report data from the same patients.

Lastly, the bibliographies of the retrieved articles were reviewed for additional studies.

scanner, built in 1974 at Washington University, USA, was 17 mm.⁵ The lower limit for the spatial resolution of a PET scanner is expected to be around 2 mm.⁶

Since January 1998, US Medicare has been authorised by the Health Care Financing Administration to reimburse costs related to the use of PET in the detection of metastatic disease in newly diagnosed, non-small-cell lung cancer (NSCLC).^{7,8} Evidence that PET is a useful tool in the diagnosis and staging of this cancer is growing, as is the number of PET centres. In 1998, there were 75 PET centres

in the USA, and there are now more than 172.⁹ By comparison there are nine centres in the UK and two in Denmark. Use of both dedicated PET and gamma-camera PET is becoming more widespread, and there is therefore a need for systematic assessment of the diagnostic value of this promising, but expensive, technology.

The aim of this study was, through a systematic review of relevant literature published after 1993, to assess the diagnostic value of dedicated PET and gamma-camera PET in discriminating between malignant and benign solitary

Table 1. Methodological quality of diagnostic accuracy studies¹²

| Grade | Criteria |
|-------|---|
| A | <p><i>Studies with broad generalisability to a variety of patients and no significant flaws in research methods</i></p> <ul style="list-style-type: none"> ● ≥35 patients with disease and ≥35 patients without disease ● Patients drawn from a clinically relevant sample (not selected to include only severe disease) with clinical symptoms fully described ● Diagnoses defined by an appropriate reference standard ● PET studies technically of high quality and assessed independently of the reference diagnosis ● Prospective study |
| B | <p><i>Studies with a narrower range of generalisability, and with only a few flaws that are well described (and effect on conclusions can be assessed)</i></p> <ul style="list-style-type: none"> ● ≥35 cases with and without disease ● Smaller range of patients, typically reflecting referral bias of university centres ● Free of other methodological flaws that promote interaction between test results and disease determination ● Prospective study |
| C | <p><i>Studies with several methodological flaws</i></p> <ul style="list-style-type: none"> ● Small sample size ● Incomplete reporting ● Retrospective study |
| D | <p><i>Studies with multiple flaws in methods</i></p> <ul style="list-style-type: none"> ● No credible reference standard for diagnosis ● Test result and determination of final diagnosis not independent ● Source of patients' cohort could not be determined or was obviously influenced by the test result |

pulmonary nodules and pulmonary masses, and in the staging of NSCLC.

Assessment of methodological quality

The search strategy retrieved about 300 references. Of these, 190 were relevant for the purpose of this study, and we reviewed these to assess eligibility for further analysis. Articles selected for inclusion met the following criteria: original work assessing the diagnostic performance of FDG-PET in the investigation of lung cancer; adequate description of methods and results; and a study population of more than ten patients. A total of 55 studies met these criteria (46 with dedicated PET and nine with gamma-camera PET).

The following information was abstracted for each eligible study: authors' names; year of publication; description of study population (number of patients, male–female ratio, age, and prevalence of lung cancer); eligibility criteria for study participants; cohort assembly (randomised, prospective, retrospective, or case control); description of imaging procedure; interpretation of scans; application of reference test; and results (sensitivity and specificity).

After masking of the authors' names, year of publication, and results, the methodological quality of the studies was assessed on the evidence-based criteria described in Table 1.

Data analysis

Most studies describe only sensitivity and specificity (nosographic probabilities), because these are most important ways of assessing the diagnostic performance of a new test. But in the interpretation of the test result, positive and negative predictive values (diagnostic probabilities) are important to the clinician. Nosographic probabilities are deemed to be relatively independent of the disease prevalence, whereas diagnostic probabilities depend on the prevalence of the disease in the study population. As prevalence falls, positive predictive value falls with it, whereas the negative predictive value rises.^{12,13}

Through calculation of the likelihood ratio, the results can be made less dependent on the prevalence of the disease. If the pretest probability and the likelihood ratio are known, Bayes' theorem or a nomogram can be used to calculate the post-test probability.¹⁴

In our study, the nosographic and diagnostic probabilities and positive and negative likelihood ratios were calculated from the reconstructed 2 × 2 tables of true-positive, true-negative, false-positive, and false-negative results. The values were calculated for each report and for the pooled data (for dedicated and gamma-camera PET, respectively). Subgroup analyses were done on the following variables: methodological quality (grades B, C, D), interpretation of PET scans (with visual qualitative criteria or semiquantitative criteria, for instance calculation of a standardised uptake value [SUV]), and gamma-camera PET versus dedicated PET. A χ^2 test was used to test whether differences between groups were significant.

Results

Descriptive analysis

Of the 55 articles eligible for further analysis, 46 addressed dedicated PET (see Webtable 1 on *The Lancet Oncology*

website <http://oncology.thelancet.com>)^{15–60} and nine gamma-camera PET (see Webtable 2, as above).^{61–69} Of these studies, 19 were not eligible for the quantitative analysis, owing to insufficient reporting of data. There were no randomised studies, and no studies met the methodological quality criteria of grade A. The distribution of the studies according to methodological quality and applied interpretation of PET results is described in Table 2.

The reported mean age was 60 years (range 56–66). There were no data on age in eight studies. The sex distribution was 71% men (range 41–99) and 29% women (range 1–59). Eleven studies reported no data on sex. The mean prevalence (pretest probability) of NSCLC was 70% (range 43–88).

Quantitative analysis

The results of the studies on dedicated PET are reported in Table 3 and those on gamma-camera PET in Table 4.

There was no significant correlation between the methodological quality of the studies (grade B, C, or D) and the diagnostic performance of PET, except for the negative predictive value of PET when used for staging NSCLC. We therefore decided to pool the values from all the studies used for diagnosis and staging separately, instead of calculating a weighted average according to grade. The values referred to are the pooled results of all eligible studies, unless otherwise stated.

The likelihood ratios were calculated for all the studies, as well as for the pooled values. Post-test probabilities for different examples of pretest probabilities were calculated for a positive and for a negative PET scan in the work-up of NSCLC (Tables 5 and 6).

Diagnosis of lung cancer

Our results indicate that dedicated PET is very sensitive (96% [SE 1]), but less specific (78% [SE 3]) in discriminating malignant from benign pulmonary nodules and masses. Both the positive and the negative predictive values were about 90%. The positive likelihood ratio was moderate (4.4) and the negative likelihood ratio was extremely low (0.05). There were no significant differences between methods of interpretation (SUV, visual, or both) in relation to the ability of PET to discriminate between malignant and benign pulmonary changes.

Table 2. Description of eligible studies

| Characteristic | Dedicated PET | Gamma-camera PET |
|--------------------------------------|---------------|------------------|
| Methodological quality | | |
| Grade A | 0 | 0 |
| Grade B | 10 | 1 |
| Grade C | 21 | 3 |
| Grade D | 15 | 5 |
| Interpretation of PET results | | |
| SUV | 10 | 0 |
| Visual | 16 | 6 |
| SUV and visual | 15 | 3 |
| Not reported | 5 | 0 |

Table 3. Diagnostic performance of dedicated PET when used to diagnose lung cancer and for N staging of NSCLC

| Diagnosis | Mean (SE) for pooled values | | | | | |
|--------------------------------|-----------------------------|-------------|-------------|-------------|-------------|-------------|
| | Sensitivity | Specificity | PPV | NPV | Positive LR | Negative LR |
| All studies (n=16) | 0.96 (0.01) | 0.78 (0.03) | 0.91 (0.02) | 0.90 (0.02) | 4.4 | 0.05 |
| Methodological quality | | | | | | |
| Grade B (n=5) | 0.97 (0.02) | 0.78 (0.04) | 0.90 (0.03) | 0.92 (0.03) | 4.4 | 0.04 |
| Grade C (n=6) | 0.97 (0.02) | 0.82 (0.04) | 0.92 (0.03) | 0.92 (0.03) | 5.3 | 0.04 |
| Grade D (n=5) | 0.95 (0.03) | 0.72 (0.06) | 0.91 (0.04) | 0.82 (0.05) | 3.4 | 0.07 |
| | NS | NS | NS | NS | | |
| Interpretation of PET images | | | | | | |
| SUV (n=4) | 0.95 (0.03) | 0.81 (0.05) | 0.90 (0.04) | 0.90 (0.04) | 4.9 | 0.06 |
| Visual (n=6) | 0.98 (0.01) | 0.71 (0.05) | 0.90 (0.04) | 0.95 (0.02) | 3.4 | 0.02 |
| SUV and visual (n=5) | 0.96 (0.02) | 0.82 (0.04) | 0.92 (0.03) | 0.91 (0.03) | 5.3 | 0.05 |
| | NS | NS | NS | NS | | |
| N staging | | | | | | |
| All studies (n=17) | 0.83 (0.02) | 0.96 (0.01) | 0.87 (0.02) | 0.95 (0.01) | 21.3 | 0.17 |
| Methodological quality | | | | | | |
| Grade B (n=5) | 0.84 (0.04) | 0.95 (0.02) | 0.90 (0.03) | 0.92 (0.03) | 17.5 | 0.17 |
| Grade C (n=5) | 0.89 (0.04) | 0.92 (0.04) | 0.89 (0.04) | 0.92 (0.04) | 10.6 | 0.12 |
| Grade D (n=7) | 0.79 (0.03) | 0.97 (0.01) | 0.82 (0.02) | 0.96 (0.01) | 26.5 | 0.22 |
| | NS | NS | NS | p<0.005 | | |
| Interpretation of PET pictures | | | | | | |
| SUV (n=3) | 0.80 (0.07) | 0.94 (0.04) | 0.82 (0.06) | 0.94 (0.04) | 14.1 | 0.21 |
| Visual (n=9) | 0.80 (0.02) | 0.97 (0.01) | 0.85 (0.02) | 0.96 (0.01) | 24.2 | 0.20 |
| SUV and visual (n=4) | 0.89 (0.04) | 0.94 (0.03) | 0.90 (0.03) | 0.94 (0.03) | 14.7 | 0.12 |
| | NS | NS | NS | NS | | |

PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio; NS, not significant. For further information concerning the likelihood ratios, see Sackett and colleagues or <http://cebmr.jr2.ox.ac.uk>

Only one prospective study compared the performance of PET versus CT in the diagnosis of NSCLC: Präuer and colleagues²¹ found sensitivity, specificity, and positive and negative likelihood ratios for CT of 100%, 52%, 2.1, and 0. The corresponding values for PET were 90%, 83%, 5.2, and 0.1.

Staging

In the staging of metastasis in the mediastinum (N stage) of NSCLC patients, we found that dedicated PET was very specific (96% [SE 1]) but less sensitive (83% [SE 2]). The predictive value of a positive PET scan was 87% (SE 2), whereas that of a negative PET scan was 95% (SE 1). The χ^2 test revealed a significant difference between the negative predictive values found by studies of grades B, C, and D ($p<0.005$): the negative predictive value was 92% in grade B/C studies and 96% in grade D studies. The positive likelihood ratio was extremely high (21.3) and the negative likelihood ratio moderately low (0.17). In their analysis of 29

studies on mediastinal staging, Dwamena and coworkers found that the mean sensitivity and specificity for CT were 60% and 77%.⁷⁰

Only nine studies addressed the use of dedicated PET for staging metastases outside the mediastinum (M staging), and only four of these reported adequate data.^{50–53} The results were promising, revealing sensitivities of 90–100% and specificities of 80–100%. However, assessment of the value of PET in the diagnosis of distant metastasis is difficult, because the number of PET-negative lesions that were actually present cannot easily be determined. What is more important is the proportion of patients in whom PET alters management, by demonstrating unsuspected metastasis or weakening suspicion of metastasis.

Bury and colleagues⁴⁶ compared PET and conventional imaging methods for the staging of NSCLC; they found that PET changed M stage in 15 (14%) of 109 patients. PET increased the stage from M0 to M1 in seven patients and

Table 4. Diagnostic performance of gamma-camera PET

| Diagnosis | Mean (SE) for pooled values | | | | | |
|-----------------------|-----------------------------|-------------|-------------|--------------|-------------|-------------|
| | Sensitivity | Specificity | PPV | NPV | Positive LR | Negative LR |
| Diagnosis (4 studies) | 0.92 (0.04)* | 0.86 (0.04) | 0.95 (0.05) | 0.80 (0.05) | 6.50 | 0.10 |
| Range | 0.77–1.00 | 0.50–1.00 | 0.91–1.00 | 0.64–1.00 | 2.00–8.10 | 0–0.3 |
| N staging (5 studies) | 0.81 (0.04) | 0.95 (0.02) | 0.79 (0.05) | 0.96 (0.020) | 17.1 | 0.2 |
| | 0.73–0.90 | 0.57–0.97 | 0.40–0.97 | 0.21–0.98 | 1.1–28 | 0.10–1.00 |

*Significantly lower than results (sensitivity) with dedicated PET ($p<0.005$).

Table 5. Relation between likelihood ratio and pretest and post-test probabilities for dedicated and gamma-camera PET

| Pretest probability (%) | Post-test probability (%) | | | |
|---|-----------------------------------|--------------------------------------|------------------------------------|-------------------------------------|
| | Diagnosis of lung cancer | | N staging | |
| | Positive PET (positive LR = 4) | Negative PET (negative LR = 0.05) | Positive PET (positive LR = 21) | Negative PET (negative LR = 0.2) |
| Dedicated PET | | | | |
| 10 | 30 | 0.4 | 70 | 2.0 |
| 25 | 55 | 1.2 | 88 | 5.5 |
| 50 | 80 | 4.5 | 95 | 17 |
| 75 | 92 | 12 | 98 | 35 |
| Gamma-camera PET (positive LR = 6.5) (negative LR = 0.1) (positive LR = 17) (negative LR = 0.2) | | | | |
| 10 | 40 | 0.9 | 60 | 2.0 |
| 25 | 68 | 3.0 | 82 | 5.5 |
| 50 | 88 | 9.0 | 93 | 17 |
| 75 | 95 | 20 | 97 | 35 |

decreased from stage M1 to M0 in eight. In another study by the same investigators,⁵² PET was compared with bone scintigraphy. In 37 of 109 cases, the two methods gave different results, and PET turned out to be correct in 35 of the 37 cases.

Gamma-camera PET

Only nine studies of gamma-camera PET were found. These few studies indicated no major difference in the performance of gamma-camera PET and dedicated PET. However, the results of gamma-camera PET varied substantially between the individual studies (Table 4).

One study⁶⁶ applied gamma-camera PET (first generation with lead collimator) and dedicated PET on the same population. In defining N stage (n=13) sensitivity, specificity, and positive and negative likelihood ratios were 40%, 63%, 1.10, and 0.96 for gamma-camera PET and 83%, 43%, 1.50, and 0.40 for dedicated PET. Shreve and coworkers⁶⁷ used dedicated PET as the diagnostic standard: gamma-camera PET diagnosed 13 of 14 masses found on dedicated PET. In the mediastinum, five of 15 metastases 0.6–1.3 cm in size and 15 of 16 metastases 1.5–3.5 cm in size found on dedicated PET were also found on gamma-camera PET.

Discussion

From this systematic assessment of the present evidence on PET in the diagnosis and staging of NSCLC, we found that there were no randomised studies, and many of the existing studies had several flaws in the methodology. Nevertheless,

the conclusions of the studies were quite consistent and apparently independent of the methodological quality.

Before reaching any conclusions, we shall discuss the following three questions, which are the backbone of the process of evidence-based decision-making.¹⁴

- Were the results in the literature valid?
- Was the evidence important?
- Is the evidence applicable in clinical practice?

The first question was partly answered above. Several studies had methodological flaws, for instance an unclear description of the eligibility criteria. This omission opens up the possibility that retrospective studies, in particular, could be associated with selection bias. Furthermore, only 65% of the studies described masked interpretation of the PET results, and 37% of the studies provided inadequate data. Finally, the application of the diagnostic standard was not clearly described in many studies, and it was not always independent of the PET result. These flaws should be avoided in future studies. However, the present evidence is consistent between the studies, and the total study population exceeded 800 patients in diagnostic studies, 1000 in studies on staging, and 400 in studies on gamma-camera PET. Furthermore, our results are consistent with those of a prospective NSCLC staging study with 102 patients,⁷¹ published after the last literature search to be included in our review was completed.

Is the present evidence on PET in the diagnostic investigation of NSCLC important? The diagnostic efficacy of a new technology can be described as a hierarchy with six levels (Table 7). The hierarchy ranges from the micro level,

Table 6. Example of the relation between the likelihood ratio and the pretest and post-test probabilities for CT obtained from a diagnostic study and a meta-analysis of staging

| Pretest probability (%) | Post-test probability (%) | | | |
|-------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| | Diagnosis of lung cancer* | | N Staging† | |
| | Positive CT (Positive LR=2.0) | Negative CT (Negative LR=0.2) | Positive CT (Positive LR=2.6) | Negative CT (Negative LR=0.5) |
| 10 | 17 | 2.0 | 20 | 5 |
| 25 | 42 | 5.5 | 45 | 12 |
| 50 | 70 | 17 | 73 | 35 |
| 75 | 85 | 35 | 90 | 60 |

*Data from reference 27. †Data from reference 70

Table 7. Hierarchy of diagnostic efficacy

| | |
|--------------------------------|---|
| 1 Technical efficacy | Description of technical imaging quality |
| 2 Diagnostic accuracy efficacy | Sensitivity, specificity, PPV, and NPV |
| 3 Diagnostic thinking efficacy | Likelihood ratio |
| 4 Therapeutic efficacy | Changes in therapeutic choices after test |
| 5 Patient outcome efficacy | Improvement in morbidity/mortality |
| 6 Societal efficacy | Cost–benefit analysis |

which concerns the physical imaging process itself, to the societal efficacy level (cost–benefit analysis).¹²

Because our aim with this review was primarily to assess the diagnostic effectiveness of PET, only studies at levels 2–3 were included in the quantitative analysis, and our conclusions on whether the evidence on PET is important is limited to these levels.

If the likelihood ratio is calculated, the results become less dependent on the prevalence. A diagnostic test with a large positive likelihood ratio or a very small negative likelihood ratio is important, because such a test produces large changes from before to after the test.¹⁴ Tables 3–6 describe the likelihood ratios for dedicated PET, gamma-camera PET, and CT. The largest gain from pretest to post-test probability was seen with dedicated PET for diagnosing (negative LR = 0.05) and staging (positive LR = 21) NSCLC. This result can be illustrated by the following examples. Patient A has a 50% pretest probability of lung cancer. After a negative PET scan, the probability of NSCLC would be only 4.5%. After a negative CT scan, the probability would be 17%. However, comparison of PET and CT for diagnosis of single pulmonary nodules is hampered by the fact that these tests are used in populations of patients with different rates of disease; for example, PET is most often applied when CT is inconclusive.

Patient B has NSCLC and a pretest probability of mediastinal metastases of 25%. After a positive PET scan showing focal FDG uptake in the mediastinum, the post-test probability of mediastinal metastases is 88%, whereas a positive CT showing enlarged lymph nodes gives a post-test probability of 45%.

The last question is whether this valid and important evidence on PET is applicable in clinical practice. The answer depends on several factors. First, the availability of the test is limited by the lack of reimbursement for clinical PET studies and the high capital investment associated with dedicated PET. If gamma-camera PET turns out to be an acceptable alternative to dedicated PET, which is still to be established, the availability might increase, because gamma-camera PET is less expensive in initial costs and working expenses. Still, both dedicated and gamma-camera PET depend on the supply of radioactive isotopes from a cyclotron.

Second, the prevalence of cancer in the population tested must be known, because the diagnostic gain from pretest to post-test probability after a PET scan depends on the prevalence. Our results indicate (Table 5) that PET, when used to discriminate between malignancy and benignity of solitary pulmonary nodules, should first be applied to populations with a prevalence of cancer between 10% and

50%. In the staging of NSCLC, the gain from pretest to post-test probability will be large, even for a low prevalence of mediastinal metastases. Studies from the USA and Switzerland indicate that a diagnostic strategy with PET and CT will be cost-effective when the prevalence is between 0.12 and 0.69, equalling savings of about US\$90–2200 per patient.^{72,73} In a recent study on the cost-effectiveness of FDG-PET for the management of solitary pulmonary nodules, Dietlein and colleagues⁷⁴ found that the FDG-PET strategy would cost EURO 3218 (US\$2831) more per life-year saved than a wait-and-watch strategy. Compared with exploratory surgery, FDG-PET would cost EURO 6912 (US\$6082) less per life-year saved. These results were calculated on the basis of an estimated PET sensitivity and specificity close to the values described above. However, the cost-effectiveness of the PET strategy was very sensitive to any changes in these values. Thus, a 7% deterioration in PET sensitivity and specificity would lead to a falling life expectancy and incremental costs, compared with exploratory surgery.⁷⁴

Finally, the diagnostic value of PET can be summarised as follows. PET is very sensitive (96%) when used to discriminate between malignant and benign solitary pulmonary nodules. If the prevalence is 50% or lower, a negative PET scan more or less rules out malignant disease (post-test probability 4.5% or less). But if PET is applied to a population with a higher prevalence (eg 70%), a negative PET would give a post-test probability of cancer of 10%, which is too high for many physicians and patients to accept without further investigation. A positive PET scan indicates a high probability of cancer (positive predictive value 91%), but because of many false-positive results (specificity 78%), further examinations would still be required.

When PET is used for mediastinal staging of NSCLC, the number of false-negative results rises (sensitivity 83%). The fact that the number of false-positive results is quite low (specificity 96%) strengthens the usefulness of PET in preoperative staging. However, because a false-positive answer could exclude the patient from a potentially curable operation, further examinations would still be required.

Conclusion

Introduction of PET as a routine diagnostic tool in the investigation of NSCLC would make it possible – with one examination – to decide whether a pulmonary nodule is malignant or benign, and to identify the stage of a potential cancer. This can be done with higher accuracy than with the current non-invasive methods. If PET is applied to a population of patients with a high prevalence of NSCLC, the PET result will in most cases be valid enough for decisions to be made on the future management of the patient, saving him or her (and society) unnecessary invasive examinations or operations.

However, studies in populations with a lower prevalence of NSCLC are recommended. Combined PET and CT scanners are now becoming commercially available, so we await studies assessing whether the combined modality leads to better diagnostic accuracy than PET alone for diagnosing and staging lung cancers.

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