

# Metabolic characterisation of solitary pulmonary nodules by positron emission tomography with FDG — preliminary report

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## Abstract

**BACKGROUND:** In the past some authors evaluated FDG-PET as a powerful tool for non-invasive assessment of malignancy of solitary pulmonary nodules (SPN). The aim of this paper is to verify the performance of positron emission tomography with fludeoxyglucose (FDG-PET) in SPN in the conditions of the Czech Republic during the first 16 months of the operation of the PET Centre Prague.

**MATERIAL AND METHODS:** The group of 22 patients with 23 SPN was investigated by dedicated PET scanner due to inconclusive CT scan. Micromorphological confirmation was available in 61%; follow-up (median = 12 months) concerned the other 39% SPN. **RESULTS:** PET was clearly positive in 11 nodules, all were malignant according to micromorphological assessment. PET was

completely negative in 10 nodules, 3 of them were micromorphologically evaluated as benign, the other 7 nodules were followed up without any signs of malignancy. In two cases, PET revealed enhanced glucose consumption, but the pattern was not typical for malignancy. These cases were considered as bronchopneumonia, but till now, they have not been definitely resolved.

**CONCLUSIONS:** Excluding two unresolved cases, sensitivity and specificity of FDG-PET was 100% for malignancy in our series. PET was helpful in medical decision-making in all patients.

**Key words:** positron emission tomography, PET, FDG, solitary pulmonary nodules, SPN

## Introduction

Solitary pulmonary nodule (SPN) is usually a casual asymptomatic radiological finding on chest radiograph or computed tomography (CT). If SPN radiologically appears malignant, open surgery follows. If SPN has benign radiological characterisation and the size is unchanged during two-year follow-up, the nodule is considered definitely benign. Sometimes radiological methods are limited to distinguishing between benign and malignant lesion. In that case micromorphology confirmation is needed by invasive investigation (transparietal or transbronchial needle biopsy or thoracoscopy or thoracotomy). In general, there are approximately 2/3 of benign SPN in patients under 35 years of age. Most malignant SPN are non-small cell lung cancer (NSCLC) — stage I — with high rate of curability (50–80%) [1, 2].

Positron emission tomography with [<sup>18</sup>F]fludeoxyglucose (FDG-PET) is a progressive, non-invasive and cost-effective [3] imaging method for metabolic characterisation of lesions. Malignant cells usually very intensively accumulate FDG, taking advantage in visualisation of malignant nodules as hot spots by PET. FDG-PET is therefore generally considered as a very sensitive tool for imaging of malignant lesions. FDG-PET specificity is some-

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times referred lower, because of FDG increased accumulation in inflammatory and granulomatous lesions.

In the past some authors evaluated FDG-PET as a powerful tool for non-invasive assessment of malignancy of SPN. The aim of this paper is to verify performance of FDG-PET in SPN in the conditions of the Czech Republic and its potential to reduce invasive diagnostic procedure.

## Material and methods

**Group of patients.** From October 1999 to January 2001 a group of 22 patients with 23 SPN was investigated by FDG-PET due to inconclusive CT scan from the point of view of biological behaviour of the lesion. The patients (12 men and 10 women, mean age 60 years) were referred to the PET Centre Prague from two University Hospitals. Suspicion of SPN originated from chest plain radiograph in all patients. Reasons for indications for radiography in this series are noted in Table 1.

**Diagnostical management.** All patients underwent spiral CT or HRCT scanning. Nodule size ranged from 1 to 6 cm, no lymph node involvement was apparent on the CT scans. Bronchoscopy was carried out in 91% (20/22) patients — (1 patient refused, 1 patient was unable to undergo invasive evaluation). CT-guided transparietal needle biopsy was carried out in 22% (5/23) SPN, only 3 were successfully targeted. Surgery was carried out in 48% (11/23) SPN, it was contraindicated in 18% (4/22) patients. In summary micromorphological confirmation was available in 61% (14/23) SPN. Follow-up (median = 12 months) concerned the other 39% (9/23) SPN.

**Method of PET scanning.** 65 minutes  $\pm$  14 minutes after intravenous administration of 525 MBq  $^{18}$ F-FDG per 70 kg (body weight corrected) started acquisition in 2D mode of entire torso and neck (5–7 bed positions) by ECAT EXACT CTI/Siemens PET scanner. Acquisition of emission data took time for 6.5 min. per bed position. Duration of hot transmission was 3.5–6.5 min. per bed position according to decreasing activity of transmission sources during their 12-month life-span. Tomographic planes were reconstructed by ECAT 7.2 software by iterative method OS-EM (6 iteration, 16 subsets, 6 mm Gaussian filter) and transitory by 7.1 software (1 iteration, 30 subsets), incl. scatter and attenuation correction using segmentation. Only seldom was filtered back projection without corrections used. Data were visually assessed by viewing of transaxial, sagittal, coronal slices and volume rendered data (maximum intensity projections).

## Results

PET was clearly positive in 11 nodules. Micromorphological assessment revealed malignant tumour in all these nodules (Table 2).

**Table 1. Characterisation of the group of patients according to the reasons for chest plain radiograph**

Frequency (%)	Reason for chest plain radiograph
5.0	Routine preoperative investigation
21.0	Dispensary (risky occupation, other cancer)
32.0	Investigation due to cough, bronchopneumonia or back pain
42.0	Asymptomatic casual evaluations

PET was completely negative in 10 nodules, three of them were micromorphologically evaluated as benign (tuberculoma, chondrohamartoma, angioliopoma). The other seven nodules were followed up for 12 months (median) without any signs of malignancy.

In two cases, PET revealed enhanced glucose consumption, but the pattern was not typical for malignancy. One patient had negative result of transthoracic needle biopsy, both patients had negative results of bronchoscopy and they are contraindicated for surgery due to bad cardiopulmonary condition. Till now, they have not been definitely resolved. Excluding these two patients, sensitivity and specificity of FDG-PET was 100% in our series (Table 3).

## Discussion

PET is referred in the literature as a reliable test for differentiating benign from malignant SPN with sensitivity and specificity in the range of 80–100%. There are uncommon tumours non-accumulating FDG, such as bronchioloalveolar carcinoma, metastatic liposarcoma, highly differentiated neuroendocrine tumours, highly fibrotic tumours with a low tumour cell density. These tumours occasionally diminish sensitivity of PET for identifying malignant SPN in larger series [2, 4–6]. In our smaller series two cases of such tumours (bronchioloalveolar carcinoma, atypical carcinoid) were present. In contrast to the literature, they avidly accumulated FDG and did not diminish sensitivity of FDG-PET in our series (Fig. 1).

Five PET positive nodules were larger than 3 cm. It is easy to find neoplasm in large nodules for PET [2]. On the other hand, three PET positive nodules were smaller than 2 cm. The employed PET scanner has the advantage in small lesion detection in comparison to questionable hybrid SPECT/PET coincidence cameras.

Resulting sensitivity should also be considered with respect to only a 12-month median period of follow-up instead of conventional > 2 years. Probably all these above-mentioned conditions enabled 100% sensitivity of FDG-PET in our study.

On the other hand, in the literature inflammatory lesions accumulating FDG are referred, e.g. coccidiomycosis, histoplasmosis, cryptococcosis, TBC and other granulomatous diseases [2]. In the Czech Republic the prevalence of these diseases is generally low. In our series only one tuberculoma was present, moreover with no FDG consumption. Probably this reason enabled 100% specificity in our study.

Two unresolved patients have chronic obstructive pulmonary disease with probable bronchopneumonia causing some stripy uptake of FDG. There is a slow regression on chest radiograph during 6 months of follow-up.

## Conclusions

In situations when anatomical imaging modalities (radiography, CT) give ambiguous results, FDG-PET seems to be a very powerful tool for characterisation of biological behaviour of SPN. Results achieved during the first 16 months of operation of the PET Centre Prague (100% sensitivity & specificity) are comparable with published papers at least. Increasing the series of patients will drop sensitivity & specificity below 100% in the future with a high probability. PET was helpful in medical decision-making in all patients.

**Table 2. Characterisation of nodules**

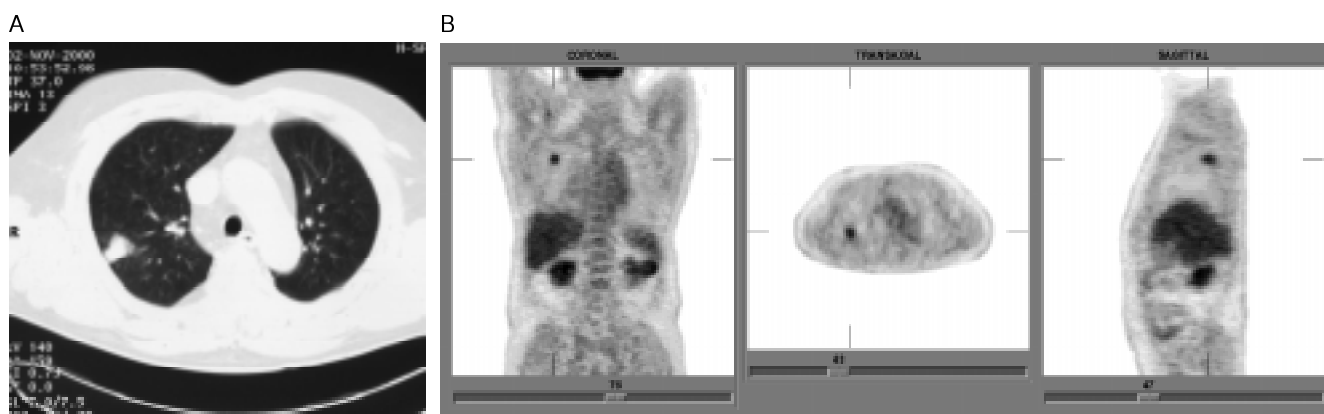
Patient number	Age	Sex	Nodule number	Nodule size [cm]	PET	Diagnosis	Kind of confirmation
1	46	F	1	Ø 1.4	-	Benign tumour	Follow-up
2	64	M	2	2.0 × 2.0	-	Benign tumour	Follow-up
3	66	F	3	1.6 × 1.0	+	Metastasis of colon carcinoma	Histology
4	65	M	4	4.5 × 5.0	+	Squamous cell bronchogenic carc.	Histology
5	62	F	5	Ø 2.5	-	Tuberculoma	Histology
6	49	F	6	4.0 × 3.0	+	Squamous cell bronchogenic carc.	Histology
7	54	F	7	Ø 1.2	-	Postinflammatory residuum	Follow-up
8	36	M	8	5.3 × 5.7	+	BALT lymphoma	Histology
9	69	M	9	Ø 3.5	-	Chondrohamartoma	Histology
10	65	F	10	1.0 × 1.3	-	Benign tumour	Follow-up
11	62	M	11	4.8 × 3.0	-	Angiolipoma	Histology
12	55	F	12	1.9 × 2.4	+	Squamous cell bronchogenic carc.	Histology
13	56	M	13	N/A	-	Bronchopneumonia of low regression	Follow-up
14	67	F	14	3.3 × 2.4	+	Bronchogenic adenocarcinoma	Histology
15	67	M	15	Ø 1.8	+	Bronchogenic adenocarcinoma	Histology
16	70	F	16	Ø 2.0	-	Postinflammatory residuum	Follow-up
17	56	M	17	3.0 × 6.0	?	Susp. bronchopneumonia	Follow-up
18	54	F	18	2.4 × 2.8	+	Bronchogenic adenocarcinoma	Histology
			19	Ø 1.0	-	Postinflammatory residuum	Follow-up
19	61	M	20	Ø 5.7	+	Bronchogenic adenocarcinoma	Histology
20	52	M	21	2.5 × 2.0	+	Atypical carcinoid	Histology
21	61	M	22	2.8 × 2.0	+	Bronchioloalveolar adenocarcinoma	Histology
22	71	M	23	5.0 × 4.0	?	Susp. bronchopneumonia	Follow-up

"Clearly negative" by PET is labelled by -; "clearly positive" is labelled by +; "positive - not typical for malignancy" is labelled by ?

**Table 3. Summarised results**

	MALIGNANT	BENIGN	UNKNOWN
PET +	11	0	0
PET -	0	10	0
PET ?	0	0	2

"Clearly negative" by PET is labelled by -; "clearly positive" is labelled by +; "positive - not typical for malignancy" is labelled by ?



**Figure 1.** Interesting case (SPN #22). On the CT (A), SPN is seen in posterior segment of upper right lobe. Nodule of 2.8 × 2.0 cm was non-homogeneous with rough margins and pleural reaction. At the PET (B), solitary focus of glucose hypermetabolism is apparent in localisation defined by CT. Of interest could be bronchoscopy with the only chronic bronchitis bilaterally and negative cytology and histology. Result of following surgery and histopathological assessment was bronchioloalveolar adenocarcinoma pT1N0M0 stage Ia.

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