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Assessment of ^{18}F-fluorodeoxyglucose dual-head gamma camera in asbestos lung diseases

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ABSTRACT: The purpose of this study was to evaluate the performance of ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography (CDET) in identifying malignant lesions in subjects exposed to asbestos.

A total of 30 patients exposed to asbestos underwent ^{18}FDG-CDET between January 2000 and June 2003. A CDET scan of the thorax and abdomen was performed 60 min after injection of ^{18}FDG in fasting patients, and results were obtained in slices in three axes. The CDET results were compared to those from computed tomography (CT), and pleural or surgical biopsy in patients with positive ^{18}FDG-CDET results.

All primary malignant mesotheliomas accumulated ^{18}FDG (n=6), and, in two patients, CDET findings were superior to those of CT, allowing early detection. In two cases, lung carcinomas with malignant pleural effusion were also detected. There were five false positive CDET results: three unilateral pleural thickening, one rounded atelectasis, and one benign lung nodule. All patients with pleural plaques showed no significant ^{18}FDG uptake. Malignant diseases were detected by ^{18}FDG-CDET imaging with a sensitivity of 89% and specificity of 71%.

Coincidence detection emission tomography can identify malignant mesothelioma in selected subjects exposed to asbestos. Coincidence detection emission tomography appears to be a useful noninvasive method for the follow-up of subjects with exposure risk of asbestosis.

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Exposure to asbestos is characterised by benign lesions: pleural plaques, diffuse pleural thickening and benign asbestos-related pleural effusion. Exposure to asbestos also results in increased risk of lung and pleural malignancies. Mesothelioma is an insidious neoplasm arising from the mesothelial surface of the pleural cavities. Mesothelioma is almost always caused by inhalation of asbestos fibres. The median survival time is 12–18 months after diagnosis [1]. Several factors are recognised as correlating with survival: initial extent of pleural disease, intrathoracic lymph node metastases, distant metastases and histological subtypes. Recently, several authors have reported that aggressive combination therapy may significantly prolong survival [2, 3]. Routinely, computed tomography (CT) and magnetic resonance imaging (MRI) are used to detect malignant mesothelioma and for tumour, node, metastasis staging [4]. Closed pleural biopsy is 50% sensitive and pleural fluid cytology shows only 32% sensitivity; therefore, biopsy can be performed with video-assisted thoracoscopic surgery (VATS). Recently, the use of positron emission tomography (PET) scanning with ^{18}F-fluorodeoxyglucose (^{18}FDG) exhibited high sensitivity for detecting mesothelioma and staging tumour involvement [5–8]. ^{18}FDG uptake is increased in metabolically active malignant cells. PET provides metabolic activity information, complementary to anatomical imaging studies. ^{18}FDG-PET is currently performed to assess the increased metabolism in tumour cells. ^{18}FDG-PET is of limited availability and high cost. A conventional dual-head gamma camera, fitted with coincidence electronic hardware (coincidence detection emission tomography (CDET)), has been developed as a less expensive alternative to dedicated PET. At the Centre Hospitalier et Universitaire de Limoges, Limoges, France, ^{18}FDG-CDET has been studied for lung cancer staging [9]. The aim of the present study was to evaluate retrospectively the usefulness of CDET in the assessment of malignant lesions in patients exposed to asbestos.

Materials and methods

Between January 2000 and June 2003, ^{18}FDG-CDET was performed in all patients referred for imaging abnormalities, such as pleural plaques or diffuse pleural fibrosis and/or asbestosis detected by chest radiography and CT. Without exclusion criteria, 30 consecutive patients were enrolled. All of the subjects had reported an occupational exposure to asbestos, mainly jobs in construction, maintenance, demolition and refractory materials. In France, asbestos workers or ex-workers are involved in medical follow-up every year. In total, 23 of the patients were currently smokers or ex-smokers (mean cumulative consumption 40 pack-yrs). Only patients with malignant mesothelioma (three out of six) presented with

dyspnoea, chest pain or pleural effusion. Physical examination, chest radiography, CT of the chest and CDET scans were obtained in all patients. At the first examination, all of the patients were given written information about CDET procedures. Additional procedures, such as diagnostic thoracentesis, closed pleural biopsy, VATS or bronchoscopy, were performed when clinically indicated.

Chest computed tomographic scan

Spiral CT examinations were performed using high-speed acquisition (Lightspeed; GE Medical Systems, Waukesha, WI, USA). The entire thorax from the apex to the costophrenic angles and upper abdomen were scanned in each patient. Continuous 5-mm slices were obtained in the hilum and mediastinum and 7-mm slices in the remaining area during the *i.v.* administration of 100 mL nonionic contrast material at 3 mL·s^{-1}. Data were analysed in a two-window setting, one for viewing the lung parenchyma and one for the pleura and mediastinum. CT image interpretation was performed separately by two radiologists blinded to any information about patients. In addition, conventional chest radiographs were read by the same radiologists. The morphological features of the pleura were analysed: pleural effusion, pleural plaques, diffuse pleural thickening (diffuse pleural fibrosis), pleural adhesion (rounded atelectasis), primary pleural tumours, and chest involvement. The lung parenchyma was analysed while detecting the characteristic findings of asbestosis: subpleural linear densities, basal fibrosis and coarse parenchymal bands. In addition, lung nodules and node mediastinal involvement were systematically checked.

Coincidence detection emission tomography acquisition and image reconstruction

All patients were asked to fast for $\geqslant$4 h prior to undergoing CDET study. Every day of CDET testing, ^{18}FDG was produced early in the morning (Flucis; CISbio International, Gif-sur-Yvette, France) and sent by means of a licensed transporter to the Dept of Nuclear Medicine, Centre Hospitalier et Universitaire de Limoges, Limoges, France. Physical activity was limited in order to minimise muscle uptake of ^{18}FDG. The capillary blood glucose level was monitored before injection. ^{18}FDG imaging started 1 h after *i.v.* injection of 150–230 MBq (4–6 mCi) ^{18}FDG. ^{18}FDG-CDET was performed using a dual-detector gamma camera (Axis; Philips Medical Systems, Cleveland, OH, USA) equipped with a 19-mm sodium iodine crystal with septa operating in coincidence mode for acquisition. Patients were imaged over the entire thorax and abdomen. Data were acquired in two-dimensional mode and decay correction was performed during the acquisition. The energy windows were set at 511 keV/30% for the fluorine-18 photopeak. A 15-ns timing window was used to acquire the coincidence events. Resolution in the axial and transaxial direction was ~7 mm. The parameters used to perform the iterative reconstruction included an expectation-maximisation maximum-likelihood algorithm with 20 iterations. Images were not corrected for photon attenuation. All of the images were evaluated for ^{18}FDG accumulation in parenchyma, pleura and hilar or

Table 1. – Characteristics of study patients

Patient No.	Age yrs	CT findings	CDET	^{18}FDG uptake$^{\#}$	Histological diagnosis
1	67	Pleural plaques	N	0	NP
2	57	Pleural thickening	P	2	Mesothelioma
3	65	Pleural plaques	N	0	NP
4	69	Pleural plaques	N	0	NP
5	48	Rounded atelectasis	P	1	Pleural fibrosis
6	69	Pleural effusion	P	2	Lung cancer
7	67	Pleural thickening	P	2	Pleural fibrosis
8	46	Pleural opacities	P	2	Mesothelioma
9	78	Pleural thickening	N	0	Sarcoma (SEF)
10	54	Pleural plaques	N	0	NP
11	58	Pleural plaques	N	0	NP
12	67	Pleural plaques	N	0	NP
13	43	Pleural plaques	N	0	NP
14	45	Pleural plaques	N	0	NP
15	48	Pleural thickening	P	1	Pleural fibrosis
16	55	Pleural plaques	N	0	NP
17	67	Pleural plaques	N	0	NP
18	77	Pleural plaques	N	0	NP
19	58	Pleural thickening	P	1	Pleural fibrosis
20	64	Pleural plaques	N	0	NP
21	75	Pleural plaques	N	0	NP
22	53	Lung nodule	P	2	Benign lung nodule
23	65	Pleural effusion	P	2	Mesothelioma
24	77	Pleural effusion	P	2	Mesothelioma
25	60	Pleural effusion	P	2	Mesothelioma
26	75	Pleural plaques	N	0	NP
27	48	Pleural plaques	N	0	NP
28	47	Pleural thickening	P	2	Mesothelioma
29	65	Lung opacity	P	2	Lung cancer
30	75	Rounded atelectasis	N	0	NP

CT: computed tomography; CDET: coincidence detection emission tomography; ^{18}FDG: ^{18}F-fluorodeoxyglucose; N: negative findings; P: positive findings; NP: not performed; SEF: sclerosing epithelioid sarcoma. $^{\#}$: grade 0, no activity; grade 1, moderate activity; grade 2, high activity.

mediastinal lymph nodes. Image analysis was performed by visual assessment of the transverse, coronal and sagittal slices, and three-dimensionally by maximum pixel ray trace mode. ^{18}FDG images were interpreted in a totally blind random fashion by two independent observers. CDET results were graded as follows: 0, absence of activity; 1, presence of moderate activity; and 2, presence of high activity. A positive CDET result was considered for grades of $\geqslant 1$. Controversial findings were solved by consensus.

Patient management

Patient-management decisions were based on the combined interpretation of CT and CDET data. Patients with a suspected malignant lesion on CT and/or CDET (positive findings) underwent diagnostic procedures, including VATS in pleural diseases, and bronchoscopy, mediastinoscopy or thoracotomy for lung diseases. All of the abnormal CDET and CT scan results were reviewed in conjunction with clinical

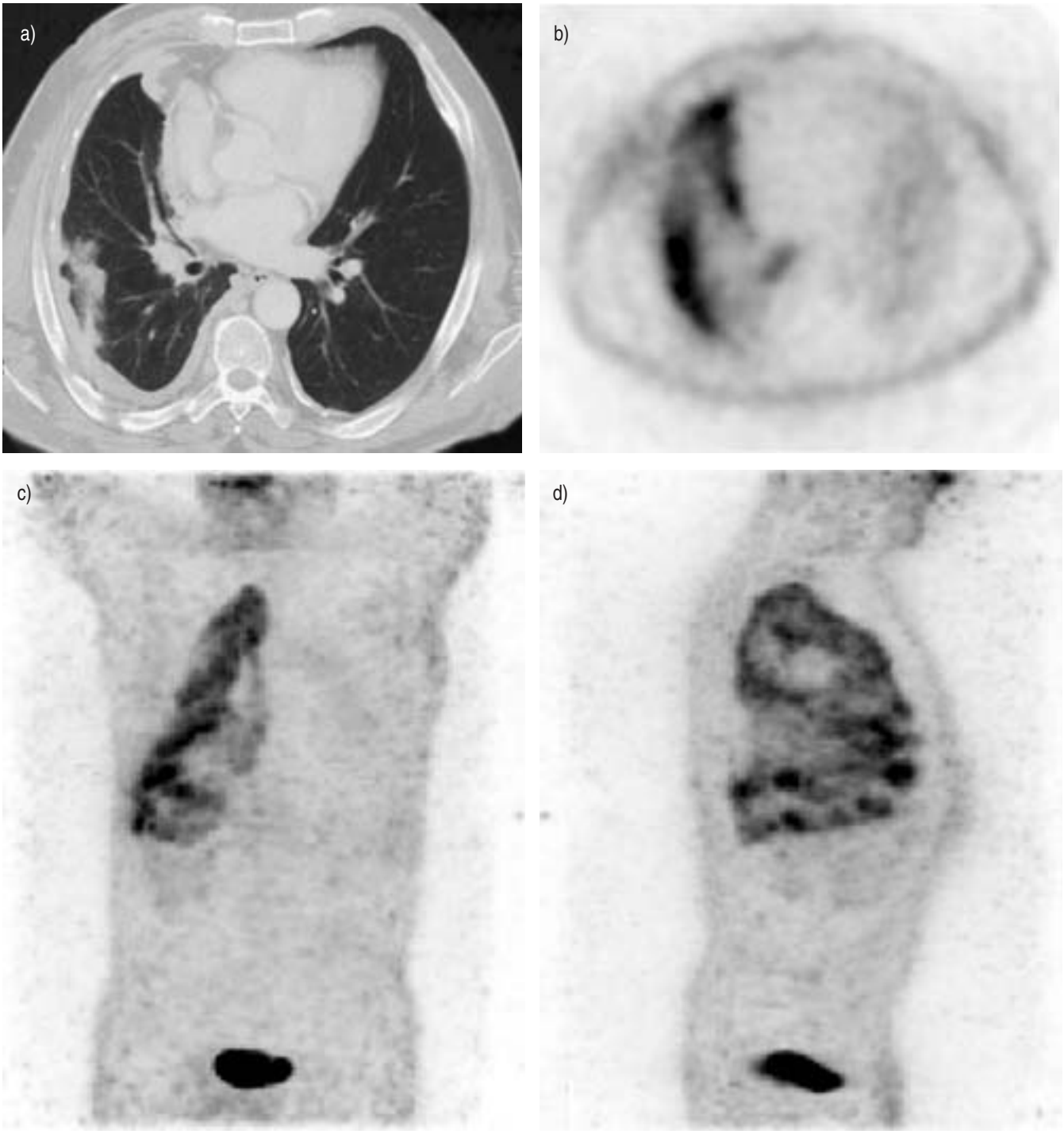

Fig. 1. – A 60-yr-old patient with epithelial mesothelioma. a) Transverse computed tomography scan slice showed right pleural thickening. b) Transverse ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography slices revealed extensive pleural involvement of pleural surfaces. Three-dimensional imaging in maximum pixel raytrace in the anterior (c) and right lateral (d) views confirmed diffuse ^{18}FDG uptake surrounding the right hemithorax.

follow-up and pathological reports from biopsy or surgical specimens. The patients with benign lesions detected by CT and/or CDET (negative findings) were followed-up at the Centre Hospitalier et Universitaire de Limoges with clinical examination, chest radiography or CT, and CDET every 6 months. The standard for deciding that a patient has a benign disease are CT scan results and negative CDET findings at 6 and 12 months.

Statistical analysis

In order to assess the accuracy of CDET in detecting malignant diseases, the true positive (TP), true negative (TN), false positive (FP) and false negative (FN) rates and sensitivity (TP/(TP+FN)) and specificity (TN/(TN+FP)) were calculated.

Results

The results of the present study are summarised in table 1. All of the 30 subjects (29 males and one female) had been occupationally exposed to asbestos. Their mean (range) age was 61 yrs (43–77). All but seven were current or former smokers (mean cumulative consumption 40 pack-yrs). The histological diagnosis was malignant mesothelioma in six patients, lung cancer in two and pleural sclerosing epithelioid sarcoma in one. In addition, CDET scanning identified increased ^{18}FDG uptake in five benign situations with histological diagnoses of rounded atelectasis in one patient, pleural fibrosis in three and benign lung nodule in one.

Of all the cancer lesions (n=9), eight were detected on ^{18}FDG-CDET images. A FN result was observed in a patient with sclerosing epithelioid sarcoma of the pleura. In four patients, malignant mesotheliomas accumulated significant amounts of ^{18}FDG (grade 2). The pattern of ^{18}FDG uptake typically matched the CT and VATS findings with regard to the extent of pleural involvement (figs 1 and 2). In addition, the presence of pleural effusion did not interfere with ^{18}FDG uptake. In two asymptomatic patients with pleural plaques, localised uptake (grade 2) of ^{18}FDG was detected (fig. 3). VATS revealed an extensive mesothelioma not identified by CT. In two cases, unilateral pleural effusion revealed significant ^{18}FDG uptake in pleura and parenchyma. Investigations revealed lung adenocarcinoma with malignant pleural effusion (fig. 4).

^{18}FDG-CDET results were falsely interpreted as positive in three patients with unilateral parietal pleural thickening (grade 1 (n=2) and grade 2 (n=1)). VATS confirmed simple

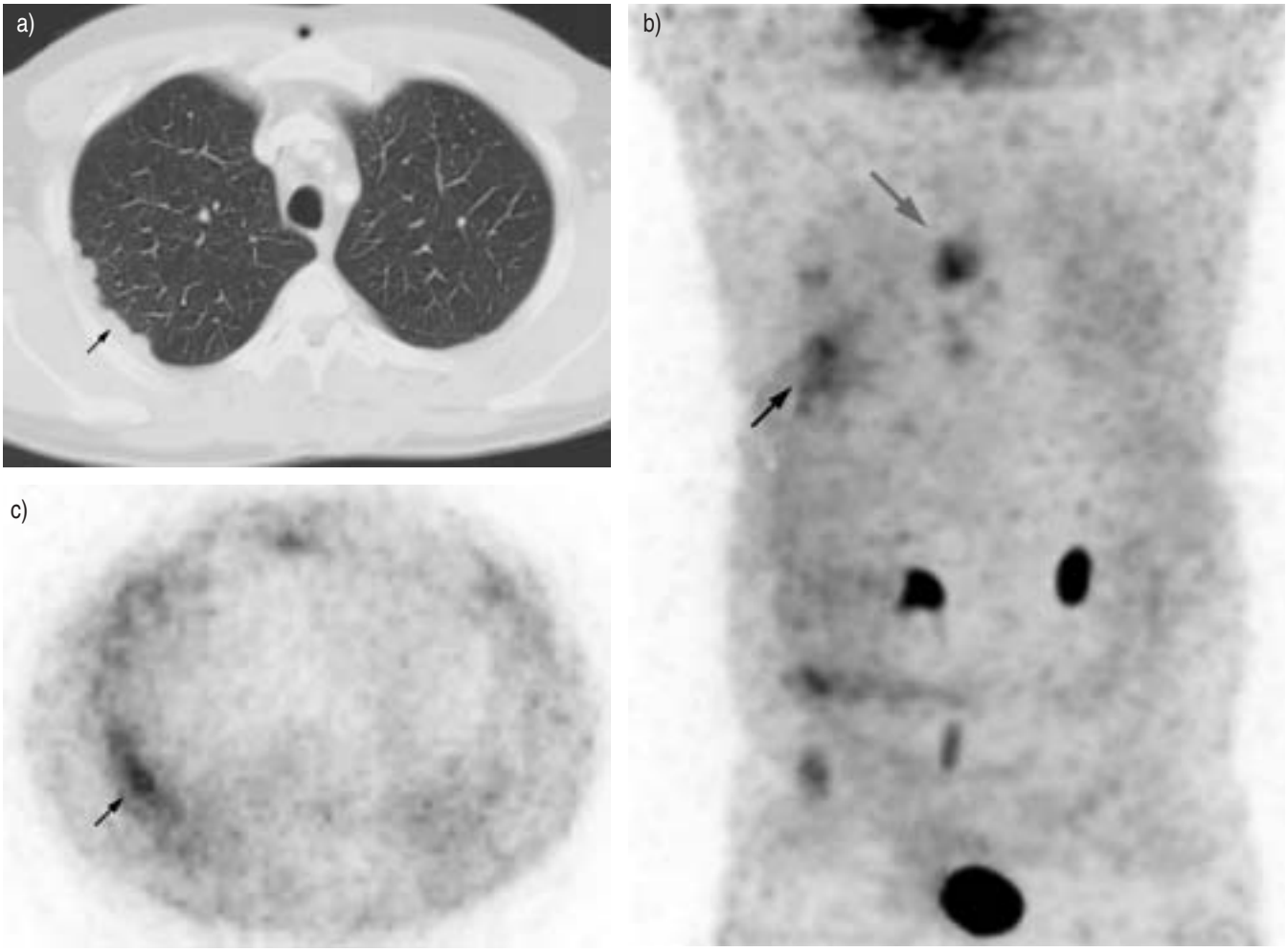

Fig. 2. – A 43-yr-old patient with epithelial mesothelioma. a) Computed tomography scan revealed right-sided nodular pleural thickening (arrow). b) Three-dimensional imaging in maximum pixel raytrace in the anterior view revealed pleural involvement (arrow) and increased focus of ^{18}FDG uptake by mediastinal lymph node (grey arrow). c) Transverse ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography images demonstrated localised pleural hypermetabolism (arrow).

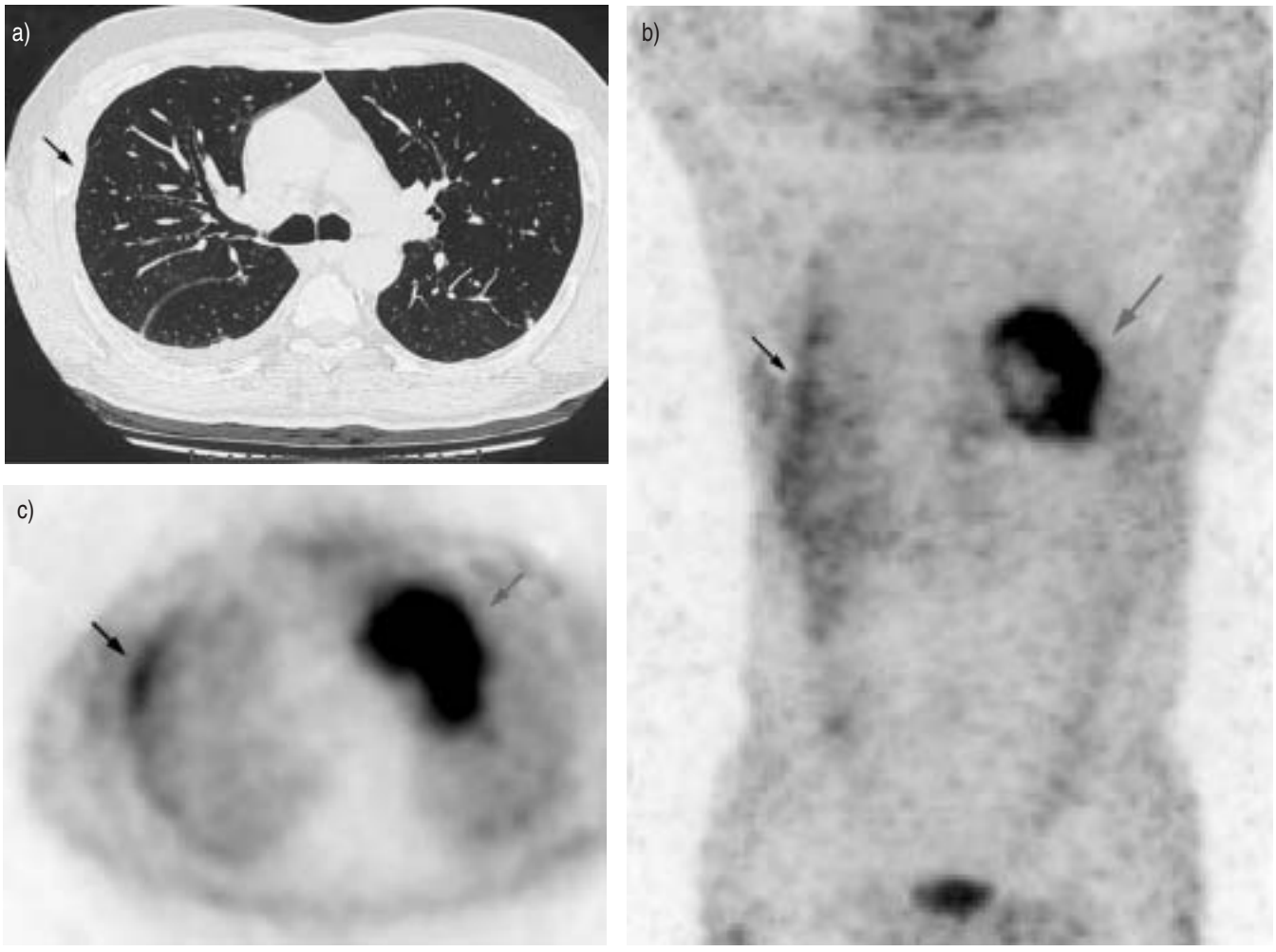

Fig. 3. – A 56-yr-old patient with pleural effusion. a) Computed tomography scan confirmed a right moderate pleural thickening (arrow). b) Three-dimensional imaging in maximum pixel raytrace in the anterior view showed localised increased of ^{18}FDG uptake on right parietal pleura (arrow) and physiological uptake of ^{18}FDG by the myocardium (grey arrow). c) Transverse ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography demonstrated localised pleural increase of tracer (arrow). There is physiological uptake of ^{18}FDG by the myocardium (grey arrow).

asbestos-related pleural thickening or fibrosis (fig. 5). Pleural plaques did not show ^{18}FDG uptake in the present subjects (n=16). In all patients with pleural plaques, ^{18}FDG-CDET was performed after a mean period of 12 months and no significant ^{18}FDG uptake was found. In another heavy smoker, CT scanning revealed a rounded atelectasis and bilateral pleural plaques with and without calcifications (fig. 6). The uptake of ^{18}FDG was moderately increased in rounded atelectasis (grade 1). VATS confirmed the presence of pleural adhesion without malignant aspect in multiple biopsy specimens. For this last patient, two consecutive CDET imaging tests had been performed at 6 and 12 months with the same result. Another FP CDET result (grade 2) was observed for a solitary lung nodule. After thoracotomy, pathology results confirmed benign granulomatosis.

Benign disease was correctly assessed in 16 out of 21 patients (five FP). Malignant diseases were detected by CDET with a sensitivity of 89% and specificity of 76% in the present study.

Discussion

The present findings suggest that ^{18}FDG-CDET could be a useful imaging method for the detection of thoracic malignancies in selected patients exposed to asbestos. CDET results were positive in all patients with malignant mesothelioma, and two malignant mesotheliomas were detected early. Unfortunately, a pleural sarcoma was not detected by ^{18}FDG imaging. In addition, two lung cancers were detected. However, five CDET results were considered to be FP: one rounded atelectasis, three diffuse pleural thickenings, and one benign lung nodule.

Imaging plays an essential role in the diagnosis and follow-up of patients exposed to asbestos. The diagnosis of pleural mesothelioma is often suggested by unilateral effusion seen on chest radiography. CT scanning is not sensitive or specific enough to differentiate between benign and malignant pleural disorders. Coronal MRI has been reported to be more specific and sensitive than CT scanning for detecting malignant pleural disease [10, 11]. ^{18}FDG-PET is also a sensitive imaging technique for distinguishing benign from malignant disorders of the pleura [5, 8].

The present results are in agreement with findings reported in ^{18}FDG-PET studies. First, BÉNARD *et al.* [4] reported that ^{18}FDG-PET is a sensitive imaging method for differentiating malignant from benign involvement in patients with asbestos exposure who present with pleural effusion or pleural thickening on CT scanning. Pleural malignant mesothelioma or malignant diseases are detected with a sensitivity of 91% and

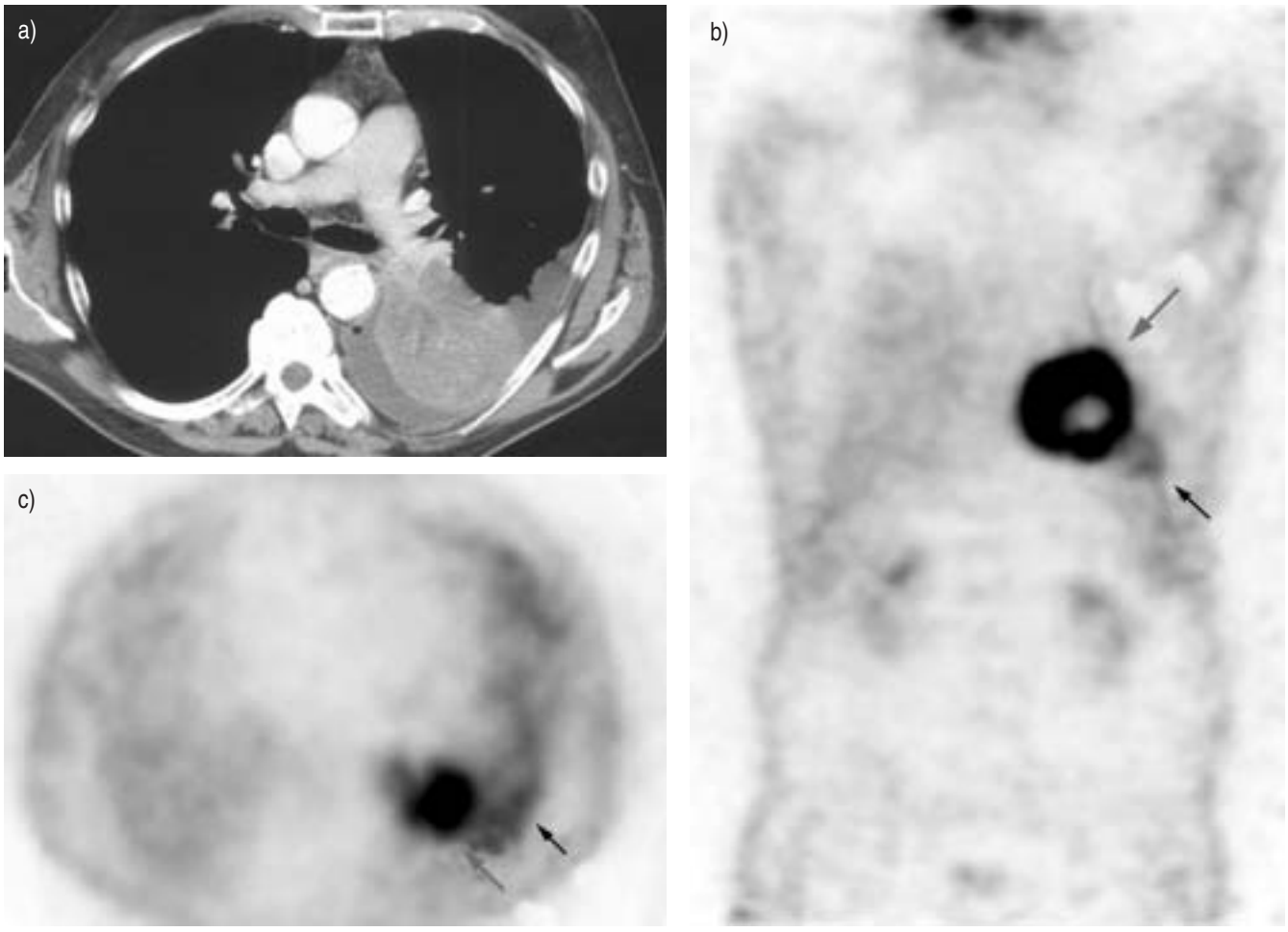

Fig. 4. – A 59-yr-old patient with pleural effusion. a) Computed tomography scan showed a left pleural effusion with primary lung cancer adjacent to the mediastinum. b) Three-dimensional imaging in maximum pixel raytrace in the anterior view confirmed lung tumour (grey arrow) and pleural involvement (arrow). c) Transverse ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography revealed ^{18}FDG hypermetabolism in the lung tumour with central necrosis photopenic area (grey arrow). In addition, there was a distinct focus on increased uptake in the posterior parietal pleura suggesting adjacent involvement (arrow).

specificity of 100%. ZUBELDIA *et al.* [6] compared CT and ^{18}FDG-PET for the evaluation of patients with known malignant mesothelioma. CT and PET were concordant in three patients, PET was superior to CT in five cases and, for one patient, CT and ^{18}FDG-PET missed local spread of a tumour to the diaphragm and pericardium. CARRETTA *et al.* [8] indicated that ^{18}FDG uptake was increased in nine out of 10 patients with mesothelioma. In the present study, ^{18}FDG-CDET demonstrated increased ^{18}FDG uptake in all mesotheliomas. In addition, sclerosing epithelioid sarcoma was detected by CT, but no ^{18}FDG uptake was observed. To the present authors′ knowledge, asbestos exposure is not associated with this rare relatively low-grade sarcoma [12]. Furthermore, ^{18}FDG-CDET results were falsely interpreted as positive in three patients with unilateral pleural thickening. In each case, VATS was performed for pleural biopsy specimens and examination of the pleural space. Histological analysis of several biopsy specimens confirmed fibrous connective tissue compatible with pleural plaques and pleural thickening. Previous studies indicate that rounded atelectasis is not metabolically active on ^{18}FDG-PET imaging [13]. In one patient in the present study, significant but moderate ^{18}FDG uptake was observed in rounded atelectasis. Moreover, talc pleurodesis before PET imaging may falsely elevate the amount of ^{18}FDG uptake [14].

In asbestos-exposed subjects, the differential diagnosis of malignant pleural mesothelioma could be difficult with inflammatory reaction, pleural thickening or benign pleural effusion. Progress has been made in CT and MRI techniques since the mid-1990s [10]. In addition, ^{18}FDG-PET provides information about metabolically active areas and may be used as a guide to the most appropriate biopsy site. Moreover, BÉNARD *et al.* [15] reported the prognostic value of ^{18}FDG-PET imaging in malignant mesothelioma, and that patients with high ^{18}FDG uptake exhibited shorter survival. SCHNEIDER *et al.* [14] confirmed that ^{18}FDG-PET detects involvement of mediastinal lymph nodes and extrathoracic sites that are underdetected by CT.

^{18}FDG-PET imaging has been reported to be of great importance in the initial diagnosis, staging and follow-up of thoracic malignancies. Owing to the high cost of a dedicated PET scanner, dual-head gamma cameras modified for coincidence detection have been proposed for oncological ^{18}FDG imaging [16–18]. More recently, CDET has appeared to be an accurate method for the diagnosis and staging of malignant mesothelioma [19]. In addition to its relatively low cost, ^{18}FDG-CDET has the advantage that it detects a wide range of photon energies, allowing its use in routine nuclear medical practice. However, CDET cannot be considered completely equivalent to full-ring PET scanners, as CDET is less sensitive and does not permit quantitative measurements.

The present results, obtained with coincidence detection

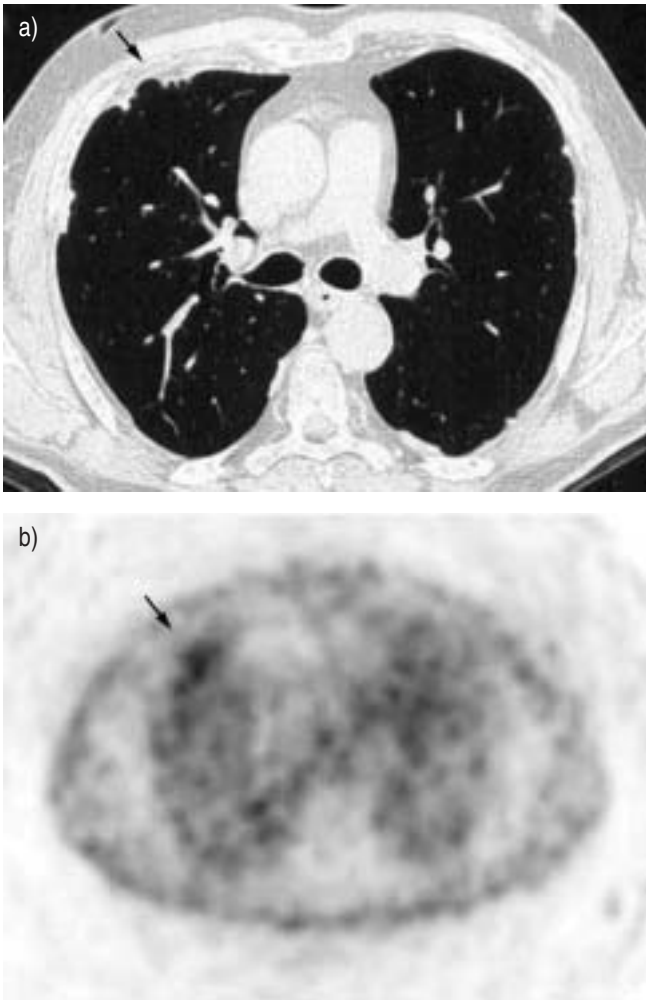

Fig. 5. – A 70-yr-old patient with benign pleural thickening. a) Computed tomography scan showed bilateral pleural thickening with and without calcifications (arrow). b) There is significant ^{18}F-fluorodeoxyglucose (^{18}FDG) uptake by pleura (arrow) in the transverse ^{18}FDG-coincidence detection emission tomography slice, but video-assisted thoracoscopic surgery confirmed the presence of pleural plaques and a diffuse thickening of the pleura with no malignant tumour cells confirmed histologically.

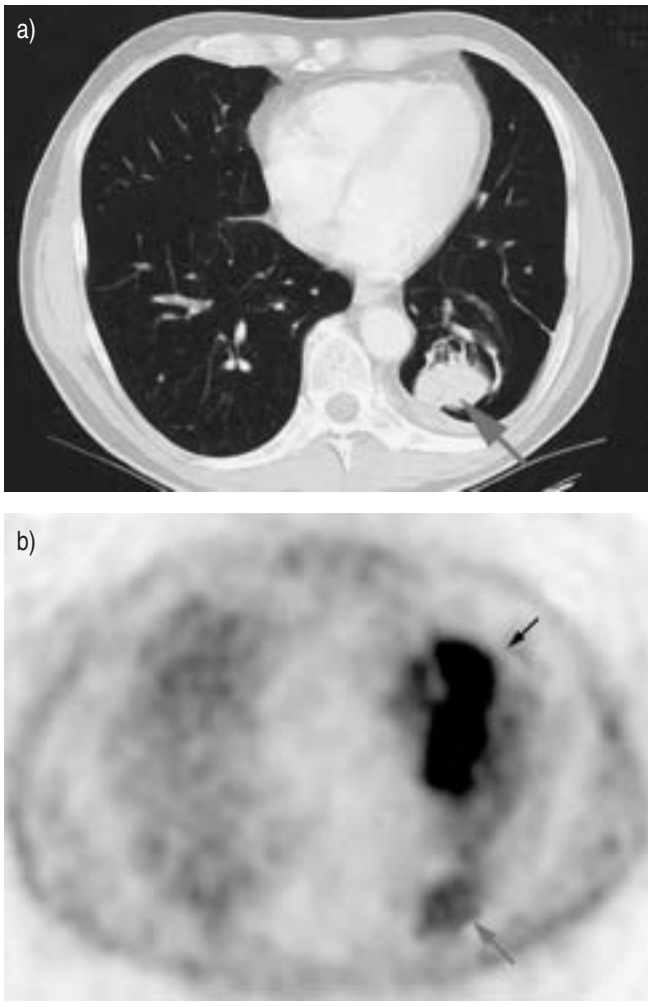

Fig. 6. – A 47-yr-old patient with rounded atelectasis. a) Computed tomography scan showed pleural plaques and rounded atelectasis (grey arrow). b) Transverse ^{18}F-fluorodeoxyglucose (^{18}FDG) imaging *via* coincidence detection emission tomography identified a moderate increased of ^{18}FDG uptake in rounded atelectasis (grey arrow). There is physiological uptake of ^{18}FDG by the myocardium (arrow).

emission tomography, require confirmation in larger series. Using coregistered morphological and metabolic data, it could be possible to detect and localise early malignant diseases in patients who have been exposed to asbestos.

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