The importance of ^{18}F-FDG PET/CT, CT and X-rays in detecting primary stage III A lung cancer and the incidence of extra thoracic metastases

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Abstract

Lung cancer (LC) has an unfavorable prognosis especially when the disease is extensive at presentation. Accurate staging is therefore needed for treatment planning of these patients. In the present study the role of positron emission tomography/computerized tomography (PET/CT) in the detection of extra thoracic metastases in LC is being evaluated. *In all 52 of our patients* with stage IIIA or lower of LC disease, a whole body ^{18}F-FDG PET/CT was performed. All patients were also subjected to general clinical evaluation, chest X- rays and chest contrast enhanced CT (CECT) and were confirmed by histopathology or magnetic resonance imaging or radiology. Incidental extra thoracic malignant *lesions were found* by ^{18}F-FDG PET/CT in 9 out of the 52 patients (17.3%). No false positive lesions were found. As for the primary LC diagnosed by fine needle aspiration cytology (FNAC): ^{18}F-FDG PET/CT diagnosed all 52 cases, CECT detected 46 cases and chest X-rays detected 28 cases. The diagnostic accuracy was 100%, 92% and 53.8% respectively. As for the 9 cases with extrathoracic metastases diagnosed by ^{18}F-FDG PET/CT they were confirmed: by biopsy 6, by MRI 2 and by X-rays with or without biopsy 2. *In conclusion*, ^{18}F-FDG PET/CT had better diagnostic accuracy in diagnosing LC stage IIIA or lower, than CECT or chest X-rays. Extrathoracic metastases were high: 9/52 as diagnosed by ^{18}F-FDG PET/CT and standardized uptake value.

Introduction

Lung cancer (LC) is one of the most common causes of death due to cancer in the world with approximately 3 million cases getting afflicted by it worldwide, accounting for 17.8% of cancer deaths every year [1]. Various diagnostic modalities are in the vogue for detecting, staging and monitoring the patients of LC [2-4]. Radiologic diagnostic modalities detect the disease based on structural changes. ^{18}F-fluoro-2deoxy-d glucose positron emission tomography/computerized tomography (^{18}F-FDG-PET/CT) detects malignant disease based on increased utilization of glucose by the cancer cells. More than 40% of the patients with LC have metastases at the time of initial presentation commonly noted in bone, brain, adrenal and renal tissue [5]. If even small distant metastatic lesions are not detected before subjecting the patient to radical surgery, more than 20% of the patients shall have a relapse of the disease [6]. We undertook this prospective study in order to evaluate the role of ^{18}F-FDG PET/CT in LC and in the detection of extrathoracic metastases of LC.

Material and methods

All 52 patients with stage IIIA or lower of LC were imaged on a Discovery STE- PET/CT scanner (GE healthcare USA). These patients included 41 males aged 40 to 72 years (mean 59 years) and 11 females aged 44 to 70 years (mean 56 years). Preoperative staging included complete patient clinical examination, chest X-rays and contrast enhanced computerized tomography (CECT) chest scan (Table 1). CT guided fine needle aspiration cytology was done to confirm the histological diagnosis of primary lesion in the lung in all patients. Magnetic resonance imaging (MRI) or chest X-rays or biopsy confirmed the extra thoracic metastases, while standardized uptake value (SUV) was measured in all these 9 patients (Table 1). All patients fasted for at least 12 h before the intravenous injection of 370 MBq of ^{18}F-FDG. The ^{18}F-FDG PET/CT acquisition was performed after 60 to 75 min of injection of radiotracer. The scanning sequence consisted of unenhanced whole body CT tomography with attenuation correction PET image, followed by the whole body ^{18}F-FDG PET/CT scan. The scanning

parameter for the unenhanced whole body CT, included 120 kV, 110 mA, 3.75 mm slice thickness and a pitch of 1.75. The PET scan was acquired in three dimensional mode with 3 min per bed position and a total of 6 or 7 bed positions.

Two nuclear medicine physicians (RS and MT) and a radiologist (MD'S) experienced in three dimensional imaging, reviewed all standard ^{18}F-FDG PET/CT images.

Results

In 9 of the 52 patients of LC extra thoracic metastases were detected in at least one organ. The metastases were found in the following organs: bone in 5 cases, brain in 2 cases, kidney in 1 case, adrenals in 1 case (Table 1).

No false positive extra thoracic lesions were found on the ^{18}F-FDG PET-CT scan. The distant extra thoracic metastases found in 9 patients were confirmed by biopsy in 6/9 cases, by MRI in 2/9 cases and by X-rays in 1/9 cases. SUV confirmed all metastases being ≥4.3. Patients with adenocarcinoma of the lung had the highest frequency of extra thoracic metastases (6/9), followed by squamous cell (2/9) and large cell carcinomas (1/9). Our findings in patients N° 3, N° 1 and N° 4 according to Table 1, are seen in Figures 1, 2 and 3 respectively.

Discussion

Contrast enhanced CT scan is commonly used in staging of LC [7, 8]. However the sensitivity, specificity and accuracy of this modality is limited [9]. There have been several studies that reported higher sensitivity, specificity and accuracy using ^{18}F-FDG PET/CT as compared to contrast enhanced CT [10-14]. Very high sensitivity from 90%-100% and specificity from 79.2%-96.4% for the detection of LC have been reported for ^{18}F-FDG PET-CT scan [4, 15-17].

By mediastinoscopy, samples from suspicious lymph nodes can also be obtained [18] for histo-pathological confir-

mation. Nevertheless not all mediastinal lymph nodes are routinely accessed, particularly those in the para-aortic region and in the aorto-pulmonary window. The limited view through the mediastinoscope and the single direction in which the biopsies can be carried, give an accuracy of approximately 90% which is surgeon dependent [18].

Ultrasound (US) and magnetic resonance imaging (MRI) were used to examine a selected anatomic region. Bone scan
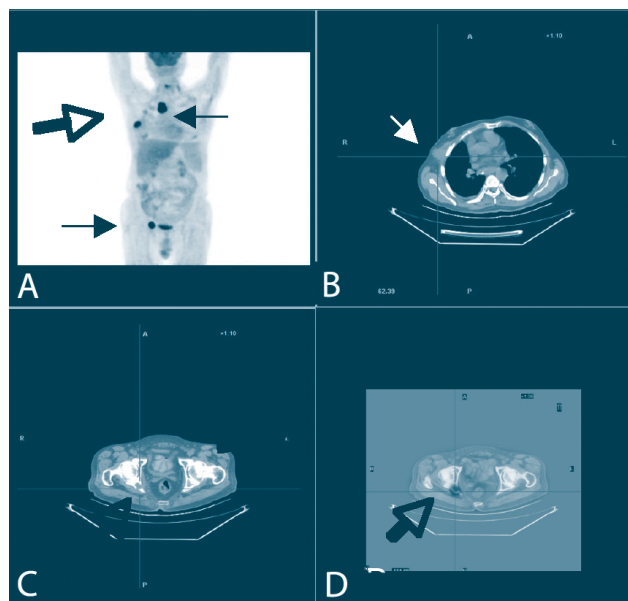

Figure 1. A: A 72 years old patient with adenocarcinoma of right lobe of the lung. The ^{18}F-FDG PET whole body scan demonstrates metastasis in the right chest wall (T3-Stage 3A) abutting the pectoralis muscles and another in the right iliac bone adjacent to the superior lip of the acetabulum. B and C: Corresponding CT scan of the chest showed the lesion in the right chest wall and a lytic lesion in the posterior pillar of the right acetabulum. D: Fused transaxial PET and CT scan image shows metastasis in the right iliac bone. Both chest wall and iliac bone lesions were metastatic as shown by histopathology.

Table 1. *Summary of the data of nine patients with documented extra thoracic metatsases*

Age/Sex /No	CECT/ Metastases	^{18}F-FDG PET-CT, LC / Metastases	SUV range of distant lesions	Confirmation test for metastases
56/F /1	Abutting on to the pleura	Right lower lobe / Cerebellar and parietal lobe	4.3	MRI-Lesion in left cerebellar hemisphere and in parietal lobe
63/M /2	Right hilar lymph nodes	Right upper lobe / second right rib	5.5	Chest X-rays- Right second rib underlying the nodule
72/M /3	Mediastinal and pectoralis muscle.	Right chest wall / pectoralis muscle and right iliac bone	9.2-22.4	Bone biopsy
63/M /4	Hilar lymph nodes	Left lobe / aorto and pericaval lymph nodes, scapula	6.3-10.5	Bone biopsy
40/M /5	Right hilar lymph nodes	Right upper lobe / right adrenal gland	12.3	Histology of adrenal gland-positive
55/F /6	Hilar lymphadenopathly	Right upper lobe / 8th thoracic vertebra	9.8	Bone biopsy
42/M /7	Mediastinal lymphadenopathy	Right upper lobe/ Left temporo-occipetal region	6.4	MRI-Left temporo-occipital lobe
53/M /8	Right upper hemithorax	Right upper lobe / right third rib	7.2-10.8	Bone biopsy
53/F /9	Enlarged hilar lymph nodes	Right suprahilar region / upper end of right tibia	8.8	Bone biopsy

M: male, F: female, CECT: contrast enhanced CT, FANC: fine needle aspiration cytology, SUV: summed uptake value, MRI: magnetic resonance imaging, Patients N° 1 and 6 had squamous cell cancer patients N 2-5 and 7 had adenocarcinoma, patient N° 8 had large cell cancer
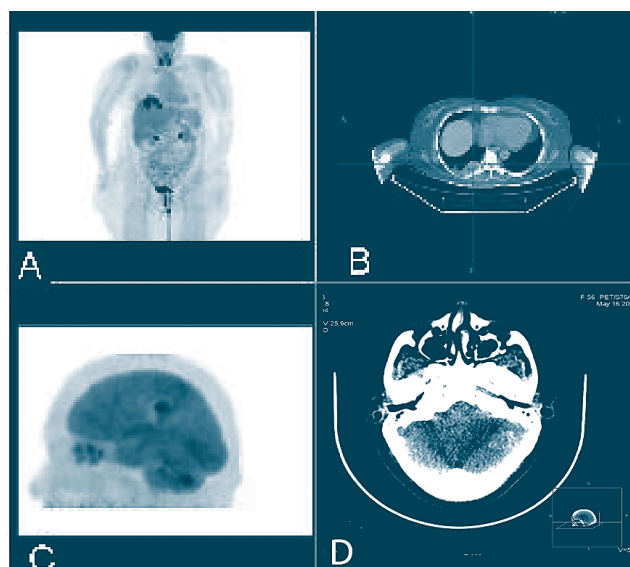
Figure 2. A: ^{18}F-FDG PET whole body scan of a 56 years old patient with squamous cell carcinoma in the right lung-lower lobe. B: Corresponding computed tomography scan shows an ill defined lesion in the right lung-lower lobe, abutting on to the pleura. C: ^{18}F-FDG PET scan shows metastases in the left cerebellar and parietal lobes of the brain. D: CT scan depicting a rounded hyper dense lesion in the left cerebellum.

Figure 3. A: ^{18}F-FDG PET whole body scan of a 63 years old patient with adenocarcinoma of the left lung. Metastatic lesions were noted at the spine of the left scapula, the aortocaval and the pericaval lymph nodes. B and C: Corresponding CT scan shows a subtle lucent area in the spine of the left scapula and widening of aorotcaval and pericaval lymph nodes. D: Fused transaxial PET and CT image depicting metastatic lesion at the spine of the left scapula. All lesions on histopathology were metastatic in nature.

is a sensitive but unspecific method, limited to the skeletal system. The ^{99m}Tc-methylene-diphosphonate bone scan has only a 14% or less chance of harboring metastatic bone disease [19-22]. As ^{18}F-FDG PET can image the whole body in a single step, it can easily detect distant metastases [23, 24] as well as ^{18}F-FDG PET/CT scan [25]. It has been reported that in stage III LC patients, ^{18}F-FDG PET scan showed extra thoracic metastases form 5%-29% [26-30]. We have found with ^{18}F-FDG PET/CT an incidence of 17.3% of distant metastases in patients with LC stage III. Sensitivity and specificity of ^{18}F-FDG PET to detect the primary LC is as high as 93% and 88% respectively [31, 32]. It has been noted that abnormal ^{18}F-FDG uptake in the chest is not always due to malignant tumor of the lung especially in our Country where high incidence false positive scans due to tuberculosis, is quite common [32, 33]. The patients included in our study were well diagnosed cases of LC, so the dilemma of false positive ^{18}F-FDG uptake was not an issue. The main effect of ^{18}F-FDG PET/CT was to diagnose the extrathoracic metastases in 9/52 patients.

In conclusion, ^{18}F-FDG PET/CT had better diagnostic accuracy in diagnosing LC stage IIIA or lower, than chest CECT or chest X-rays. Extrathoracic metastases were high 9/52 as diagnosed by ^{18}F-FDG PET/CT and SUV.

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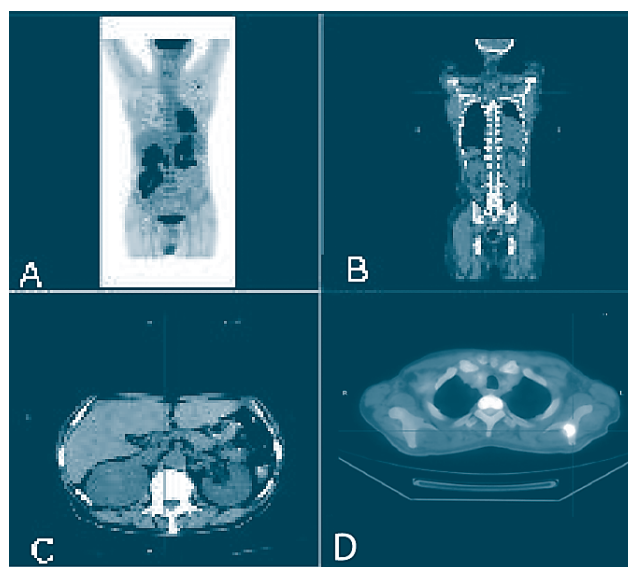2. Pfannenberg AC, Aschoff P, Brechtel K et al. Value of contrast-enhanced multiphase CT in combined PET/CT protocols for oncological imaging. *Br J Radiol* 2007; 80 (954): 437-445.
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