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Comparison of [^{18}F]FDG-PET and L-3[^{123}I]-iodo-α-methyl tyrosine (I-123 IMT)-SPECT in primary lung cancer

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Objective: The aim of this study was to evaluate L-3[^{123}I]-iodo-α-methyl tyrosine (IMT)-SPECT and FDG-PET in pulmonary lesions suspected to be lung cancer. ***Methods:*** Whole body PET (measured transmission corrected emission scans) was performed 45 minutes after i.v. injection of 222–370 MBq (6–10 mCi) ^{18}F-FDG on a Siemens PET scanner (ECAT EXACT 47) including 5–6 bed positions. ^{123}I-IMT-SPECT (chest) was performed after injection of 370 MBq (10 mCi) with a dual head camera (Picker Prism 2000) and commercially available reconstruction algorithms. Ten patients (6 male and 4 female) with suspected lung cancer were investigated. The results were compared to histological findings after surgery or bronchoscopic biopsies and CT. ***Results:*** ^{123}I-IMT-SPECT and FDG-PET were able to detect all 9 cases of lung cancer (1–8 cm in diameter). One case was true negative. Both imaging methods were true positive with respect to mediastinal lymph node metastases in one patient. The tumor/background ratio was higher with PET (8.20 vs. 2.84). ***Conclusion:*** Despite the limited number of patients it may be concluded that IMT-SPECT as well as FDG-PET are suited to correctly diagnose lung cancer. Nevertheless, FDG-PET, if available, seems to be better suited because of the higher tumor/background ratio and better resolution.

Key words: ^{123}I-IMT, ^{18}F-FDG-PET, lung cancer

INTRODUCTION

LUNG CANCER is the prime cause of death from malignant diseases and it is still increasing. It is unquestioned that early detection of a tumor and the presence of metastases has significant influence on therapy. Local recurrence and restricted mediastinal lymph node involvement would be treated by surgical revision and often radiation therapy whereas distant metastases would require chemotherapy and/or local radiation therapy. A number of imaging methods are now used to detect the presence and location of lung cancer as well as lymph node involvement. Only a few radiopharmaceuticals have gained importance in clinical imaging such as ^{67}Ga, ^{201}Tl and monoclonal antibodies but imaging with these tracers is limited due to low tracer uptake and the resolution of gamma cameras. FDG-PET has proven its ability to distinguish various types of lung cancer from benign lesions,[1] but acute inflammatory processes are a significant drawback. Recent reports have demonstrated that ^{123}I labeled amino acids like L-3[^{123}I]-iodo-α-methyl tyrosine (IMT) may also be used for imaging of brain tumors.[2] Because tumor proliferation is not only associated with enhanced glucose consumption, but also protein synthesis, labeled amino acids have been suggested for tumor imaging[3] but the number of patients was small, even though a wide range of various tumor types had been covered. The aim of this study was to evaluate IMT-SPECT in detecting lung cancer and its lymph node or distant metastases as compared to FDG-PET.

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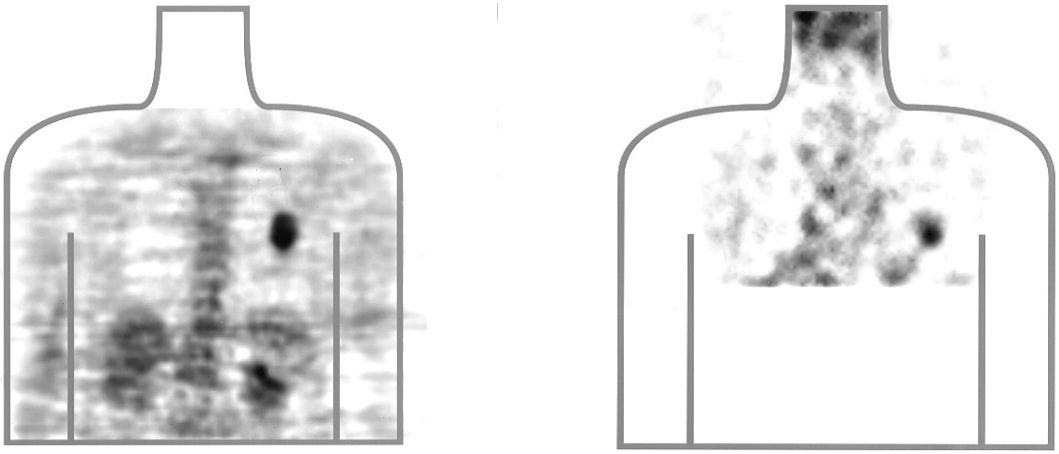
MATERIALS AND METHODS

Patients

Ten patients (6 male and 4 female, age 58 ± 12 years) with



A B

Fig. 1 A: FDG-PET scan (coronal view) shows a large area with intense FDG accumulation located in the middle field of the left lung (patient No. 7). B: IMT-SPECT (coronal view) of the same patient shows increased tracer accumulation in the same area. Histologically, this area represents a non-small cell lung cancer.

Table 1 Patients characteristics

Patient	Sex	Tumor histology	FDG-PET		IMT-SPECT	
			SUV	T/B* ratio	T/B SPECT	T/B Planar
1	F	lung cancer (NSCLC)**	11.2	7.1	2.8	1.02
2	M	lung cancer (NSCLC)	0.5	7.7	2.8	1.02
3	F	lung cancer (SCLC)***	1.8	2.6	2.1	1.4
4	M	lung cancer (NSCLC)	13.8	9.3	3.2	1.3
5	F	lung cancer (NSCLC)	5.2	9.3	3.1	1.2
6	F	lung cancer (SCLC)	6.4	9.1	2.9	1.05
7	M	lung cancer (NSCLC)	4.6	13.4	4.4	1.1
8	M	lung cancer (SCLC)	2.4	3.5	2.7	1.1
9	M	lung cancer (NSCLC)	5.1	11.8	1.6	1.2
			5.66	8.20	2.84	1.15
10	M	Benign lesion (hamatoma)	1.8	1.5	1.1	1.0

* T/B: tumor-to-background ratio
** non-small cell lung cancer = NSCLC
*** small cell lung cancer = SCLC

suspected lung cancer were enrolled presurgically. The patients had follow-up for up to 12 months. In 9 cases, lung cancer was histologically confirmed (surgery: n = 5, bronchoscopy: n = 4). Two independent observers classified FDG-PET and IMT-SPECT images as positive or negative for tumor tissue. Uptake of FDG and IMT was evaluated visually and also quantitatively by calculating the ratios of tracer accumulation in the lesion to the unaffected contralateral regions of reference with the region of interest (ROI) method. Circular ROIs were drawn around the tumor and the reference area of the contralateral thorax.

IMT-SPECT

Radiolabeling

IMT was prepared by means of a modified iodogen kit procedure with 250 μg methyl tyrosine (Fluka) in 500 (μ*l* acetate buffer (0.15 M; pH = 4.7) and about 370 MBq of purified ^{123}I iodide[4,5] in 1 m*l* of saline which were transferred to an iodogen-coated vial. The electrophilic substitution reaction was allowed to proceed for 2 minutes at room temperature of the reaction solution. After sterile filtration of the reaction solution an additional 2 m*l* of sterile PBS buffer was added. The radiochemical yields exceeded 90%.

Quality Control

HPLC qualitity control was performed on a reversed phase column (250 × 4 mm) and a linear gradient elution over 30 minutes from a 100% aqueous solution [Triethylammonium-phosphate (TEAP); 0.7%, pH 2.5] to 100% methanol. The radiochemical purity was always higher than 94%.

SPECT

Images were obtained 1 hour after i.v. injection of 222–370 MBq ^{123}I with a double-head camera (Picker Prism 2000). Planar images of the chest were obtained in anterior and posterior views. Additionally, a SPECT-study of the chest was performed (3 degrees, 30 sec per step, step and shoot, 180°) immediately after planar imaging. The image matrix was 128 × 128. The data were processed by filtered back projection with a Butterworth filter and a cut-off frequency of 0.4.

FDG-PET

^{18}F-deoxyglucose (FDG) was commercially obtained from a research center (Karlsruhe, Germany). Whole body studies were performed with a dedicated PET scanner (ECAT EXACT, Siemens/CTI). The patients were fasted overnight to reduce serum insulin levels. About 250–370 MBq ^{18}F-FDG was injected intravenously and flushed with 20 m*l* saline solution. The patients were in a complete resting condition at the time of injection and during the waiting period. Emission scans were obtained 45–60 minutes after the injection. For attenuation correction, measured transmission scans (7 minutes per bed position) were used. Tomograms were reconstructed by filtered back projection with a Hanning filter (cut off frequency 0.4/cycle, decay correction, no scatter correction). The image matrix was 128 × 128.

RESULTS

IMT-SPECT and FDG-PET were able to detect all 9 cases of lung cancer (1–8 cm in diameter) (Table 1). One case was true negative. Both imaging methods were true positive with respect to mediastinal lymph node metastases in one patient. The tumor/background ratio (T/B) was higher with PET (8.20 vs. 2.84), so that the tumors were better delineated with FDG-PET.

No significant differences between NSCLC and SCLC could be found with respect to T/B ratios and SUVs. Above all, no correlation between T/B ratios and SUVs could be found.

DISCUSSION

FDG-PET has proven to be a gold standard in diagnosing malignant lung tumors[1,6] with a sensitivity of 93 to 100% but PET is still of limited availability. Therefore, functional SPECT imaging tracers are desirable. For this reason, we studied IMT. ^{123}I-IMT is a modified amino acid. Although it is recognized by a specific amino acid transporter, it is not integrated into proteins. Therefore, it has been suggested to investigate the amino acid transport rate for tumor detection which is assumed to be increased in neoplasms.[2,3]

Our data demonstrate that IMT was able to detect all primary tumor sites as well as mediastinal lymph node metastases in one patient. Furthermore, one benign lesion (hamartoma) did not show uptake of IMT. Semiquantitative analysis showed that the tumor-to-background ratio of the SPECT images was in the range of 1.5–4.4. The benign lesion showed a tumor to background ratio of 1.1. No major difference in IMT-uptake was evident when comparing small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Both groups showed significantly higher uptake levels than the benign lesions or normal lung tissue. Our results support the primary observations of Jager et al.[3] who examined extracranial tumors including two NSCLC and one SCLC.

Direct comparison of the results obtained with FDG-PET demonstrated that all lesions detected by IMT-SPECT were also visualized by FDG-PET. The major difference was the higher image qualitiy due to higher resolution and enhanced uptake ratios for FDG. This finding could be substantiated by semiquantitative assessment. T/B ratios of FDG were in the range of 2.6–17.1 versus 1.5–4.4 in IMT. Interestingly, T/B ratios as well as SUVs in FDG-PET were not significantly higher in NSCLC than in SCLC. This might be due to the small number of patients since this has not been observed by other groups.

Our data indicate that IMT-SPECT seems to be useful for detecting SCLC as well as NSCLC lung cancer and might even play a role in the differentiation of malignant versus benign lesions in solitary pulmonary lesions.

CONCLUSION

Despite the limited numbers of patients, it may be concluded that IMT-SPECT is useful for the staging of lung cancer as well as the differentiation of solitary lung nodules. Nevertheless, FDG-PET, if available, seems to be better suited because of the better tumor/background ratio and better resolution.

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