ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Sep; 20 (9): 800-804
http://www.simm.ac.cn; www.chinainfo gov.cn/periodical

^{99m}Tc-MIBI single-photon emission-computed tomography in diagnosis of lung cancer and mediastinal metastasis lymph nodes

SHEN-TU Yang[1], ZHOU Yun-Zhong, ZENG Jun[2] (*Department of Thoracic Surgery*; [2]*Department of Nuclear Medicine, Shanghai Chest Hospital, Shanghai 200030, China*)

KEY WORDS lung neoplasms; mediastinal neoplasms; lymph nodes; technetium compounds; single-photon emission-computed tomography

ABSTRACT

AIM: To evaluate the value of technetium-99m-methoxyisobutyl isonitrile (^{99m}Tc-MIBI) single-photon emission-computed tomography (SPECT) in diagnosis of lung cancer and in preoperative prediction of mediastinal metastasis lymph nodes. **METHODS**: After the chest image of ^{99m}Tc-MIBI SPECT, fifty patients (40M, 10F; age 56 a ± 11 a) diagnosed "lung field shadow" underwent the lung focus and mediastinal lymph nodes resection. As the golden standard, pathologic diagnosis was used to evaluate the role of preoperative ^{99m}Tc-MIBI SPECT. **RESULTS**: The sensitivity, specificity, and accuracy of ^{99m}Tc-MIBI SPECT were 93 %, 50 %, and 86 %, respectively in lung cancer and 81 %, 95 %, and 88 %, respectively in mediastinal metastasis lymph node. The results were also better than those of chest scan with CT. **CONCLUSION**: The ^{99m}Tc-MIBI SPECT is a useful and noninvasive method for diagnosing lung cancer and predicting mediastinal metastasis lymph nodes, which will guide the surgeon to resect the mediastinal metastasis lymph nodes.

INTRODUCTION

As we knew, the enlargement or swelling of mediastinal lymph nodes did not always indicate the tumor cell penetration, sometimes they were lymphadenitis or lymphogranuloma. The values of CT scanning to predict the mediastinal metastasis lymph nodes were unsatisfactory, about 73 % of sensitivity and 60 % of specificity[1]. Although thoracoscopy or mediastinoscopy could offer quite accurate diagnosis, the patients would suffer much more trauma and pay extra money. The nuclear image was sometimes used as an assist method for diagnosis of the lung carcinoma. But due to the old technique of plane acquisition and the "blood pool" overlap, the general scintigraphic image or gamma cameras often fail to expose the adjacent structure of carcinoma clearly, especially the mediastinal metastasis lymph nodes, so, we surgeons always had no choice and had to resect all of the mediastinal lymph nodes to avoid leaving out the metastasis lymph nodes, however, this strategy was easy to cut the non-penetrated lymph nodes[2]. The postoperative pathologic examination showed that many resected mediastinal lymph nodes were not metastasis of cancer cell. It was considered that the resection of normal mediastinal lymph node would weaken the patients' tumor cell immune function.

The single-photon emission-computed tomography (SPECT) had a better result for detecting the lung focus and mediastinal lymph nodes[1,3-5], we observed some cases diagnosed "lung field shadow" who underwent chest image with technetium-99m-methoxyisobutyl isonitrile (^{99m}Tc-MIBI) SPECT to find a practical and noninvasive method for distinguishing the lung lesion and guiding surgeons to resect the mediastinal metastasis lymph nodes.

MATERIALS AND METHODS

Patients Fifty patients in our department during 1997 Mar-Oct were enrolled randomly in this study. The primary diagnosis, "lung field shadow" was set up by the X-ray film of chest, 40M, 10F, age 56 a ± 11

[1] Correspondence to Dr SHEN-TU Yang.
Phn 86-21-6282-1990, ext 3801. Fax 86-21-6280-1109.
E-mail sxzheng@server.shcnc.ac.cn
Accepted 1999-05-07

a, ranged from 28 to 73 a. The preoperative examination included routine laboratory tests, chest plain film radiography, CT scanning of the thorax and cera, fiberoptic bronchoscope with biopsy, whole body skeleton ECT, pulmonary function tests, ECG, and ^{99m}Tc-MIBI SPECT of chest. None of the patients received preoperative radiotherapy or chemotherapy. Every patient was operated. The thoracic surgery included VATS (only one patient), lobectomy, and pneumonectomy merge resection of the mediastinal lymph nodes. The location of lymph nodes refered to the lung and mediastinal lymph node's distribution drawing (supplied from National Cancer Center, Japan). All samples of lung focus and lymph nodes were examined by one experienced pathologist of the Pathological Department of Shanghai Chest Hospital.

Scintigraphic technique The MIBI box was offered by the manufacturer, Wuxi Nuclear Research Institute, Jiangsu Province, China (1 mg MIBI/box). The radiopharmaceutical with technetium-99m (1110 Mbq/mg MIBI) was prepared by the Nuclear Department of our hospital. This procedure was according to the manufacturer's instruction. Each patient was injected ^{99m}Tc-MIBI 740 – 1110 MBq intravenously. Scintigraphic acquisition started 15 min and 2 – 3 h after tracer injection. The data were acquired by using a Siemens Multispect-2 type double-head gamma camera, the parameters were 60 frames over 3600, 128 × 128 matrix, gamma ray > 300,000 counts per frame. The initial acquired data were reconstructed with computer and the transaxial, coronal, and sagittal slices image of chest were obtained. The experienced radiologist observed and evaluated the images, then gave a report or some suggestion to our surgeons about the location of cancer focus and mediastinal metastasis lymph nodes.

The quote of diagnostic tests The chest images were compared with the postoperative pathological results which were as the golden standard and listed in the tables of diagnostic test about the lung cancer and mediastinal metastasis lymph node, respectively. With counting the ratio, we gained the quotations of sensitivity, specificity, accuracy, positive. and negative predictive values.

RESULTS

Contrasting to the postoperative pathological results, there were lung cancers in 42 patients out of 50 cases. Other 8 patients had no lung tumor (tuberculosis in 2, pneumonia in 3, abscess bronchiolitis in 1, fibrosis in 1, and mediastinal tumor in 1). In lung cancer, histopathological results included squamous cell carcinoma and adenocarcinoma.

Lung focus There were 43 patients who showed the positive results of image with ^{99m}Tc-MIBI SPECT. Among them, there were lung cancer in 39, pneumonia in 2, mycetogenic pneumonia in 1, and tharoma in 1 (Tab 1).

Tab 1. The data of diagnostic test and the diagnostic role of SPECT on lung cancer.

		Pathology +	Pathology −	
SPECT	+	39 (a)	4 (b)	43 (a+b)
	−	3 (c)	4 (d)	7 (c+d)
	Total	42 (a+c)	8 (b+d)	50 (*n*)
Sensitivity		(39/42) 93%		
Specificity		(4/8) 50%		
Accuracy		(43/50) 86%		
Positive predictive value		(39/43) 91%		
Negative predictive value		(4/7) 57%		

Formula of the quote: Sensitivity = a/(a + c); Specificity = d/(b + d); Accuracy = (a + d)/N; Positive predictive value = a/(a + b); Negative predictive value = d/(c + d).

Mediastinal lymph node All mediastinal lymph nodes of the 42 patients (lung cancer) were examined. In 37 cases, the pathological results were the same as the preoperative SPECT reports (positive in 17 cases, negative in 20 cases). (Tab 2)

DISCUSSION

The ^{99m}Tc-MIBI SPECT had obvious improvement in two major aspects, first, technetium-99m-MIBI could combine unspecifically with tumor cell; second, the double-head ECT could reconstruct the chest images in three slices (transaxial, coronal, and sagittal). So, the ^{99m}Tc-MIBI SPECT could either indicate the nature of chest neoplasm or manifest the conceal mediastinal metastasis lymph nodes which were near the trachea,

ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Sep; 20 (9)
E-mail aps@server shcnc ac cn Phn/Fax 86-21-6474-2629

Tab 2. The data of diagnostic test and the diagnostic role of SPECT on mediastinal metastasis lymph node.

		Pathology +	Pathology −	
SPECT	+	17 (a)	1 (b)	18 (a+b)
	−	4 (c)	20 (d)	24 (c+d)
	Total	21 (a+c)	21 (b+d)	42 (*n*)
Sensitivity			(17/21) 81%	
Specificity			(20/21) 95%	
Accuracy			(37/42) 88%	
Positive predictive value			(17/18) 94%	
Negative predictive value			(20/24) 83%	

Formula of the quote: Sensitivity = a/(a + c); Specificity = d/(b + d); Accuracy = (a + d)/N; Positive predictive value = a/(a + b); Negative predictive value = d/(c + d).

arch, and esophageal (# 3, # 4, # 5, # 6, # 9 group). Otherwise, the surgeons could view any slice of chest images with the unique advantage of SPECT (3D reconstruction images). Our study showed that the SPECT had a high sensitivity of 93 % in diagnosing the pulmonary lesion, but only low specificity of 50 %. The previous report indicated the highest specificity reaching to 100 %[1]. We analyzed the reason of false negative cases. In the first case, the start time of scintigraphic acquired over 3 h. The report was not reliable. In other two cases, the pulmonary lesions were quite small ($1.5 \times 1.0 \times 0.5$ and $2.3 \times 2.3 \times 2.0$, respectively), which may cause the gamma camera hardly to detect the focus' radioactivity. In spite of this, as a functional imaging, we thought at first that there were the prime multidrug-resistance to P-glycoprotein in tumor cells. The size of lymph node was not the most important aspect. As we knew, the P-glycoprotein could clean the ^{99m}Tc-MIBI inside tumor cells[6]. So, we considered that it was compatible to add ^{201}Ti-MIBI imaging for those patients in order to improve the diagnostic specificity of SPECT. Some authors suggested that this method make up the short point of Technetium-99m [excessive speedy][4,5]. We thought it may be useful to some suspicion patients. We had some idea to compare the value of the two nuclei in single with combined using for suit patients.

There were 3 cases diagnosed the inflammatory disease in 4 false positive cases. What is the cause? In general, due to the abound supply of blood, the inflammatory focus could aggress the nucleus to create the positive imaging. Using old gamma camera technique, which only had the plane image of lung focus, the image of inflammatory focus and tumor showed the same positive mass. But now, with the advantage of the SPECT, when analyzing the early and delayed images, we could see that the delayed image was more tinge (often looklike the cloud or thin slide) than that of early inflammatory focus; then the tumor focus always showed a clear mass in two stage. The second, rotating the 3D reconstruction image, we could see the inflammatory focus showing a strip-like picture when rotated to an angle, indicating the diffuse and thin disease; however, the lung cancer lesion continuously showed a ball or mass shape, reflecting the density and aggressive focus (Fig 1, 2).

These two points prompted that the ^{99m}Tc could combine with the tumor in more long time than that of inflammatory focus, and mean time, the 3D reconstruction image could distinguish the shape difference between the two focus. If we pay attention to the overmention points, the false positive result could be decreased. As the other report, our study showed that the SPECT imaging had no significance in different pathological type of lung cancer[1]. In our study, 28 cases' images of mediastinal lymph nodes were consistent with their pathologic diagnosis, so the sensitivity was 81 %. The 4 false negative cases' lung lesion was bigger and near the left hilar, it closed or merged to the mediastinal lymph nodes. There is possibility of missing the metastasis lymph nodes in reading the image photos. Besides, the left side is easier to be influenced by the cardiac blood pool radioactivity which can interfere the founding of lymph node. So, when we read these image, more attention should be paid to the mediastinal lymph node near the cardiac pool. We surgeons should assist to read the image of SPECT to increase the accuracy in resecting the mediasinal lymph node. Compared with the foreign report of higher sensitivity (91 %)[1,3], on the one hand, SPECT examination just began in our country, and needs more experience; on the other hand, SPECT has a wonderful future in prospecting the positive mediastinal lymph node. Besides, whether

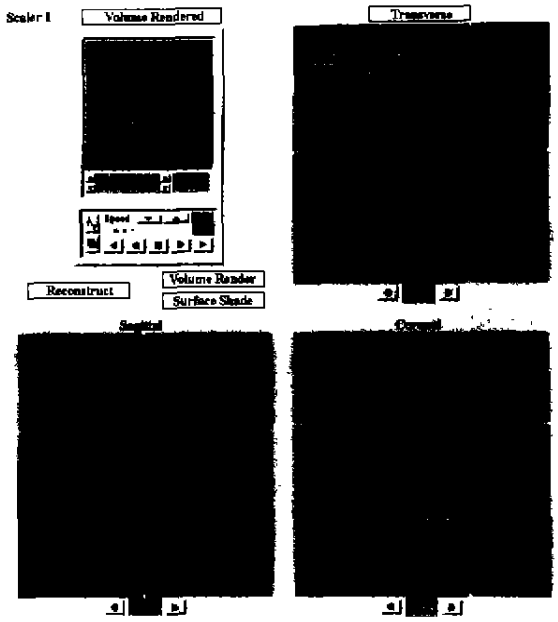

Fig 1. ^{99m}Tc **SPECT early image of a patient. The left upper lobe mass can be seen in each slice and reconstruction image, preoperative diagnosis: lung cancer (false positivity case). Pathological diagnosis: pneumonia.**

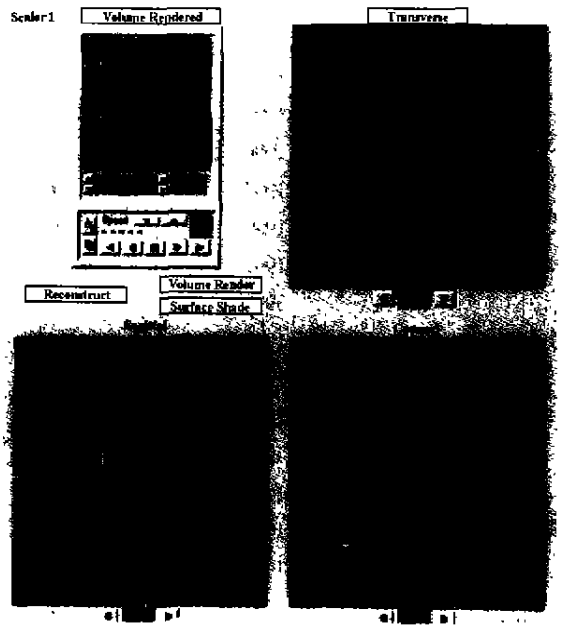

Fig 2. Delayed image of the same patient, the focus was more tinge than that in early image. Rotating the 3D reconstruction image to a slice, the focus showed a strip-like picture.

the number of metastasis lymph node and invading field have some correlation with the SPECT positive image are worth studying further. In recent years, the metastasis mediastinal lymph nodes on the lung lesion opposite side (N_3) have been paid a lot of attention, which are important to help the surgeon to stage and choose the operation fashion. We can use the advantage of SPECT in clinic to avoid unnecessary invading examination and operation. In our study, only one case has false positive image, the cause of false positive image is still unclear, maybe the lymphositis, but no pathologic certification.

CONCLUSION

According to our study, SPECT has a unique value in diagnosing lung cancer and in prospecting the metastasis mediastinal lymph nodes, which supply a new method to help to resect the lymph nodes accurately and quantitatively. With more experience of SPECT in clinic, the diagnostic power of SPECT must be obviously increased. The SPECT should play its proper role in thoracic surgery.

REFERENCES

1 Chiti A, Maffioli LS, Infante M, Grasselli G, Incarbone M, Gasparini MD, *et al*. Assessment of mediastinal involvement in lung cancer with technetium-99m-sestamibi SPECT. J Nucl Med 1996; 37: 938 – 42.
2 Naruke T, Goya T, Tsuchiya R, Suemasu K. Importance of surgery to non-small cell lung carcinoma of lung with mediastinal lymph node metastasis. Ann Thorac Surg 1988; 46: 603 – 10.
3 Salvatori M. Advances in pulmonary nuclear medicine. Rays 1997; 22: 51 – 72.
4 Nishiyama Y, Kawasaki Y, Yamamoto Y, Fukunaga K, Satoh K, Takashima H, *et al*. Technetium-99m-MIBI and thallium-201 scintigraphy of primary lung cancer. J Nucl Med 1997; 38: 1358 – 61.
5 Takekawa H, Itoh K, Abe S, Ogura S, Isobe H, Furudate M, *et al*. Thellium-201 uptake, histopathological differentiation and Na-K ATPase in lung adenocarcinoma. J Nucl Med 1996; 37: 955 – 58.
6 Piwnica-Worms D, Chiu ML, Budding M, Kronauge JF, Kramer RA, Croop JM. Functional imaging of multidrug-resistant P-glycoprotein with an organotechnetium complex. Cancer Res 1993; 53: 977 – 84.

ISSN 0253-9756 Acta Pharmacol Sin 中国药理学报 1999 Sep; 20 (9)
E-mail aps@server.shcnc.ac.cn Phn/Fax 86-21-6474-2629

锝 99m-MIBI 单光子发射型计算机体层摄影术对肺癌及纵隔肿瘤转移淋巴结的诊断

申屠 阳[1]，周允中[1]，曾 骏[2]（[1]上海胸科医院胸部外科；[2]核医学科，上海 200030，中国）

关键词 肺肿瘤；纵隔肿瘤；淋巴结；锝化合物；单光子发射型计算机体层摄影术

目的：探讨^{99m}Tc-MIBI SPECT 对肺癌及纵隔转移淋巴结的术前评估价值. **方法**：对照 50 例"肺部阴影待查"患者术后病理与术前^{99m}Tc-MIBI SPECT 显像结果，获取相关诊断试验指标. **结果**：^{99m}Tc-MIBI SPECT 对肺癌和纵隔转移淋巴结的诊断敏感性、特异性、准确性分别为93 %，50 %，86 %和 81 %，95 %，88 %. **结论**：^{99m}Tc-MIBI SPECT 对术前诊断支气管肺癌并预测纵隔转移淋巴结有较高的应用价值，对手术中定向摘除转移淋巴结具有实际指导意义.

（责任编辑 朱倩蓉）