

□ 원 저 □

Thallium-201 SPECT in the Evaluation of Postoperative Tumor Recurrence on the Chest Wall in Lung Cancer

Young Hoon Ryu, M.D., Hyung Jung Kim, M.D.¹, Chul Min Ahn, M.D.¹,
Se Kyu Kim, M.D.¹, Hyo Chae Paik, M.D.², Doo Yun Lee, M.D.²,
Kyung Young Chung, M.D.², Mijin Yune, M.D., Sang June Park, M.D.,
Sung Wook Moon, M.D., Sang Jin Kim, M.D., Jong Doo Lee, M.D.

*Division of Nuclear Medicine, Department of Diagnostic Radiology,
Department of Internal Medicine¹, Department of Chest Surgery²,
Yonsei University College of Medicine, Seoul, Korea**

=국문초록=

폐암 수술 후 흉벽의 종양 재발 검출에 있어 Tl-201 폐 SPECT의 유용성

유영훈, 김형중¹, 안철민¹, 김세규¹, 백효채², 이두연²,
정경영², 윤미진, 박상준, 문성욱, 김상진, 이종두

연세대학교 의과대학 진단방사선과학교실, 내과학교실¹, 흉부외과학교실²

Background : 본 연구의 목적은 폐암 수술 후 흉벽의 종양 재발 검출에 있어 Tl-201 폐 SPECT의 유용성을 평가해보고자 하였다.

Methods : 총 28명의 환자를 대상으로 하였고 이중 14명의 수술 후 흉벽에의 폐암의 재발이 추적 CT 검사에서 의심이 되었던 환자 10명의 방사선학적, 이학적소견과 흉수의 세포검사모두에서 양성으로 판명된 수술 후 흉막 삼출을 보이는 환자군과 4명의 만성 결핵성 농흉 환자군을 대조군으로 포함하였다. 모든 환자군에서 111 MBq의 Tl-201을 정맥 주사 후 30분과 4시간후에 전신 평면 영상과 흉곽에 대한 SPECT를 시행하였다. 종양의 Tl-201섭취는 2명의 판독자에 의하여 다음의 4단계로 나누어 평가하였다; no uptake:0, similar to contralateral lung:1, higher than contralateral lung but less than heart:2 and similar to heart:3.

This study was supported by a faculty research grant for Yonsei University College of Medicine for 2001 (No. 2001-19)

Address for correspondence :

Young Hoon Ryu M.D.

Division of Nuclear Medicine, Department of Diagnostic Radiology

Yongdong Severance Hospital, Yonsei University College of Medicine,

Kangnamgu Dogokdong 146-92, 135-720, Seoul, Korea.

Tel : 82-2-3497-3518 Fax: 82-2-3462-5472 E-mail : ryuyh@yumc.yonsei.ac.kr

Results : 수술 후 흉벽에의 폐암의 재발이 추적 CT 검사에서 의심이 되었던 환자 14명 중 13명에서 Grade 3또는 2의 강하게 증가된 Tl-201의 섭취를 보였다. 그리고 14명중 2명에서는 CT에서 관찰되지 않았던 다른 부위의 종양 재발을 확인 할 수 있었다. 반면에, 양성 수술 후 흉막 삼출군에서는 섭취가 없거나 (8/10) 또는 허탈된 폐에 미미한 (grade 1) Tl-201의 섭취만을 보였다. 만성 결핵성 농흉군에서는 비교적 균일하게 경계를 보이는 미약한 정도의 (grade 1 or 2) Tl-201의 섭취를 보였다.

Conclusion : Tl-201 폐 SPECT는 폐암 수술 후 흉벽의 종양 재발 검출에 있어 CT에서 제공하는 형태학적인 정보이외의 종양 재발에 관한 기능적 정보를 더 제공하며, PET이 없는 기관에서 사용 가능한 유용한 방법이 될 수 있을 것으로 생각된다. (*Tuberculosis and Respiratory Diseases* 2002, 53:542-549)

Key words: Lung, Neoplasm, Recurrence, Thallium-201, SPECT.

Difficulties are encountered in the detection of tumor recurrence on chest wall in patients treated for lung cancer. Computed tomography (CT) is currently the imaging method of choice in following up of patients who treated lung cancer. However, current imaging studies including CT provide valuable information but it is usually no specific enough to aid in the clinical management. Therefore, many patients undergo invasive procedures to determine the tumor recurrence and help guide patient care after treatment for lung cancer.

Several PET studies have confirmed that FDG-PET is reasonably good predictors of residual tumor or tumor recurrence¹⁻³. Patz et al showed a sensitivity of 97% and specificity of 100% for FDG-PET in distinguishing tumor recurrence from residual fibrosis in 38 patients treated for bronchogenic cancer³. However, FDG-PET remains a relatively expensive and complicated procedure and is available at only a very limited number of sites.

Several studies have been performed to investigate the use of Tl-201 imaging in the detection of malignancy⁴⁻⁸. The potential clinical

utility of Tl-201 is probably related to its mechanism of localization, which passes intracellularly to viable tumor, although mechanism of Tl-201 uptake are not clearly defined⁸. Moreover, attempts had been made to distinguish tumor recurrence and radiation fibrosis especially in brain tumors⁹⁻¹¹.

In this work, we report the result of the studies designed to evaluate the tumor recurrence of chest wall in patients who underwent treatment for bronchogenic carcinoma and were suspected for tumor recurrence on chest wall or were found to have residual or newly developed abnormalities on chest radiographs or CT scan. This study focused on the ability of Tl-201 SPECT imaging for the detection of the postoperative tumor recurrence on chest wall and for differentiation malignant from benign pleural effusion.

PATIENTS AND METHODS

28 patients (21 male, 7 female; age 38-69 years) including 10 with suspected recurrence of tumor in the chest wall on postoperative chest CT scan,

Table 1. Postoperative chest CT findings of each groups

CT findings	Suspected tumor recurrence	Benign postoperative effusion	Chronic tuberculous empyema
Operation			
Pneumonectomy	11	9	0
Lobectomy	3	1	0
Pleural thickening			
Irregular	14	4	2
Smooth	0	6	2

10 with postoperative pleural effusion which proved benign on radiologic, cytologic and laboratory findings, and 4 with chronic tuberculous empyema as control group were included. Patients who were suspected tumor recurrence on chest wall or had benign postoperative pleural effusion had performed pneumonectomy or lobectomy for lung cancer 9 to 25 months prior to Tl-201 lung SPECT. Tl-201 SPECT and chest CT scan were performed within a week. Suspicion of tumor recurrence was based on a deteriorating clinical course, a suspicious change in CT examination, or both. Informed consent was given by all patients. Chest CT scans were obtained with GE 9800 scanner (General Electrics, Milwaukee, WI, USA). Continuous 1-cm-thickness sections were obtained at 1-cm interval from the lung apices to the adrenal glands. Contrast material (Optiray 320, Mallinkrodt Medical Inc., Quebec, Canada) was intravenously administered (total amount, 100ml). A SPECT study of the lung was obtained 30 minutes and 4 hours after intravenous injection of 111MBq (3mCi) of Tl-201 on a dual-headed gamma camera (ADAC, Milpitas, CA) equipped with a high-resolution, low-energy parallel hole collimator. Sixty-four projections with an acquisition time of 40 sec/view were acquired in 64 X

64 matrices with a 5.6-degree of angular increment. The images were reconstructed with a filtered back projection method using a Butterworth filter (cut-off frequency of 0.35 cycle/cm at order no.5). Attenuation correction was not performed. Thallium activity of the tumor was visually graded by two nuclear medicine physicians and scored as follows: no uptake:0, intensity similar to that of the contralateral lung:1, higher than that of the contralateral lung but less than that of heart:2 and similar to that of the heart:3. In two patients, follow-up Tl-201 SPECT was performed after radiation therapy of the recurrent tumor mass on the chest wall to evaluate treatment response.

RESULTS

Clinical data and radiological findings including postoperative chest CT scan of all patients are summarized in Table 1.

Initial agreement was complete between two readers in the interpretation of each of the Tl-201 SPECT scan except one patient, which was resolved by consensus. In early SPECT images taken 30 minutes after intravenous injection of Tl-201, markedly increased Tl-201 uptake was

Table 2. Tl-201 SPECT findings of each groups

Tl-201 SPECT findings	Suspected tumor recurrence	Benign postoperative effusion	Chronic tuberculous empyema
30 minutes SPECT			
Grade 3	11	0	0
2	2	0	1
1	1	4	3
0	0	6	0
4 hours SPECT			
Grade 3	10	0	0
2	3	0	0
1	1	4	4
0	0	6	0
Pattern of uptakes			
Focal, Irregular	14	0	0
Diffuse, Smooth	0	2	4

noted in all patients with suspected recurrence of tumor in the chest wall, grade 3 in eleven patients and grade 2 in two patients (Table 2, Fig. 1A, B). In two patients who had received radiation therapy for the recurrent tumor mass on the chest wall after initial Tl-201 SPECT, follow-up SPECT 3-4 weeks after cessation of radiation therapy revealed disappearance of increased thallium uptake (Fig. 1C). In other two patients, Tl-201 SPECT depicted additional recurrent tumor mass lesions that were barely perceptible on chest CT scan (Fig. 1B, D). No significant difference was noted in uptake of Tl-201 by the recurrent tumor between early and delayed SPECT. Of those 14 patients in whom recurrence of the tumor on chest wall was suspected, 8 patients performed biopsy and confirmed the recurrence of the tumor. Whereas no (8 patients) or grade 1 (2 patients) uptake along the collapsed lung were seen in patients with postoperative benign pleural effusion (Table 2, Fig. 2). Patients with chronic tuberculous

empyema showed increased Tl-201 uptake as well, but in lesser degree (grade 1 or 2), when compared to recurrent tumor uptake, and depicted relatively smoothly margined increased uptake along the chest wall in all four patients.

DISCUSSION

Response to therapy is continually reassessed with imaging studies such as chest radiography, CT and MRI. These modalities provides important anatomic and morphologic information but cannot always help distinguish residual or recurrent tumors from benign post-treatment changes^{12,13}. Some patients may undergo a biopsy to determine tumor viability, although invasive procedures, which include transthoracic needle biopsy, pleural biopsy and open lung biopsy, have associated risks. These procedures, however, do not always provide a definite answer, particularly when residual abnormalities are seen on radiographs, because sampling errors may occur. A new,

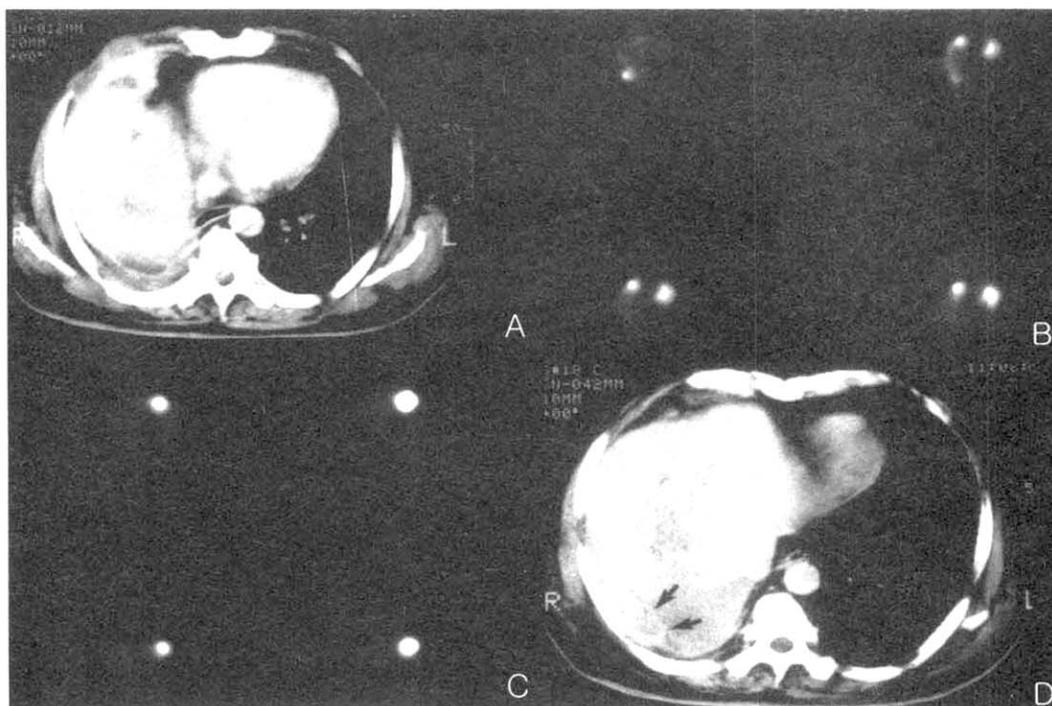


Fig. 1. 60-year old male patient who had received right pneumonectomy 1 year ago for known squamous cell carcinoma. Postoperative chest CT scan revealed irregular marginated chest wall mass with enhancement on anterior and posterior chest wall (A). 4-hour delayed SPECT images showed grade 3 increased Tl-201 uptakes on anterior and posterior chest wall which were corresponded to chest CT scan abnormalities (B). However, additional focus of grade 3 increased uptake was depicted on lower posterior thorax and meticulous retrospective review of chest CT scan showed another recurrent tumor mass lesion (D). The patient had received radiation therapy for the recurrent tumor mass on the chest wall after initial Tl-201 SPECT, follow-up SPECT 3-4 weeks after cessation of radiation therapy revealed complete disappearance of previously increased uptakes (C).

noninvasive technique with the ability to help assess treatment efficacy would be invaluable.

Tl-201 has been used to evaluate the tumor viability since it passes intracellularly to viable tumor. The mechanism of thallium uptake in tumor cells, although details have not been entirely elucidated. Several studies have been performed to investigate the use of Tl-201 imaging in the detection of malignancy and

Tl-201 chloride has been described as a positive indicator for lung neoplasms irrespective of histology. Differentiation of tumor recurrence from benign postoperative changes is important in the management of patients who treated lung cancer. Attempts have been made to distinguish tumor recurrence and post-treatment changes using thallium-201 SPECT in brain tumors and found useful in the evaluation of treatment response⁹⁻¹¹.

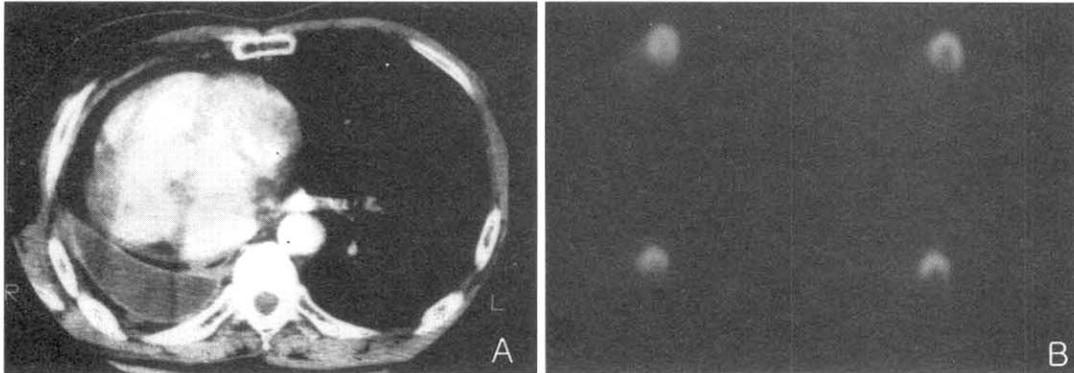


Fig. 2. 57-year old male patient who had received right pneumonectomy 2 year ago for known squamous cell carcinoma. Postoperative chest CT scan revealed small amount pleural effusion without evidence of chest wall mass or abnormal focal thickening or enhancement of pleura or chest wall (A). 4-hour delayed SPECT images showed no abnormal increased Tl-201 uptakes on chest wall (B).

Several PET studies have confirmed that FDG-PET is reasonably good predictors of residual tumor or tumor recurrence^{1,3,14,15}. However, FDG-PET remains a relatively expensive and complicated procedure and is available at only a very limited number of sites. The technology needed to perform SPECT with Tl-201, on the other hand, is widely available and cost-efficient. Moreover, in a study of Kahn et al about recurrent brain tumor, they demonstrated no statistically significant difference in sensitivity or specificity between the Tl-201 SPECT and FDG-PET¹¹.

On the basis of these considerations, we performed Tl-201 lung SPECT for the evaluation of tumor recurrence and benign postoperative changes. The results of our study showed that recurrent tumor on chest wall revealed significantly increased thallium uptake, whereas benign postoperative pleural effusion or tuberculous empyema revealed no or faint smoothly margined uptake of thallium.

Although other entities can cause an increase of Tl-201 uptake¹⁶, our results suggest that Tl-201 lung SPECT can play an important role in guiding patient care after treatment for lung cancer and, if necessary, can direct biopsy for pathologic confirmation. Tl-201 SPECT more accurately represents post-therapy viable tumor burdens than do other imaging modalities such as CT. Thus, at this time, we consider abnormal findings on postoperative Tl-201 SPECT after operation to be indicative of tumor recurrence until proven otherwise. Patients with residual abnormalities on radiographs and normal findings on Tl-201 SPECT scans will almost certainly be considered as absence of tumor recurrence.

In conclusion, Tl-201 lung SPECT seems to be useful to detect postoperative tumor recurrence on chest wall and to differentiate malignant from benign pleural effusion and may provide additional information to the morphologic data obtained by CT.

Summary

Purpose : The purpose of our study was to assess the usefulness of the Tl-201 SPECT for the detection of the postoperative tumor recurrence on chest wall.

Methods : 28 patients including 14 with suspected recurrence of tumor in the chest wall on postoperative chest CT scan, 10 with postoperative pleural effusion which proved benign on radiologic, cytologic and laboratory findings, and 4 with chronic tuberculous empyema as control group were included. All patients underwent SPECT 30 minutes and 4 hours after intravenous injection of 111MBq of Tl-201. Tumor uptake was visually graded by two interpreters and scored as follows : no uptake:0, similar to contralateral lung:1, higher than contralateral lung but less than heart:2 and similar to heart:3.

Results : Markedly increased (grade 3 or 2) Tl-201 uptake was noted in patients with suspected recurrence of tumor in the chest wall (13/14) whereas no (8/10) or minimal (2/10) uptake along the collapsed lung in patients with postoperative benign pleural effusion. In two patients, Tl-201 SPECT revealed additional recurrent tumor mass lesions that were barely perceptible on chest CT scan. Patients with chronic tuberculous empyema showed relatively smoothly marginated increased uptake along the chest wall (4/4), but lesser in degree (grade 1 or 2), when compared to recurrent tumor uptake.

Conclusion : Tl-201 lung SPECT seems to be useful to detect postoperative tumor recurrence on chest wall and to differentiate malignant from benign pleural effusion and may provide additional

information to the morphologic data obtained by CT.

REFERENCES

1. Ichiya Y, Kuwabara Y, Sasaki M, Yoshida T, Omagari J, Akashi Y, et al. A clinical evaluation of FDG-PET to assess the response in radiation therapy for bronchogenic carcinoma. *Ann Nucl Med* 1996;10:193-200
2. Erasmus JJ, McAdams HP, Patz EF. Non-small cell lung cancer: FDG-PET imaging. *J Thorac Imaging* 1999;14:247-56
3. Patz EF Jr, Lowe VJ, Hoffman JM, Paine SS, Harris LK, Goodman PC. Persistent or recurrent bronchogenic carcinoma: detection with PET and 2-[F-18]-2-deoxy-D-glucose. *Radiology* 1994;191:379-82
4. Tonami N, Shuke N, Yokoyama K, Seki H, Takayama T, Kinuya S, et al. Thallium-201 single photon emission computed tomography in the evaluation of suspected lung cancer. *J Nucl Med* 1989;30:997-1004
5. Lee JD, Lee BH, Kim SK, Chung KY, Shin DH, Park CY. Increased thallium-201 uptake in collapsed lung: a pitfall in scintigraphic evaluation of central bronchogenic carcinoma. *J Nucl Med* 1994;35:1125-8
6. Suga K, Kume N, Orihashi N, Nishigauchi K, Uchisako H, Matsumoto T, et al. Difference in ²⁰¹Tl accumulation on single photon emission computed tomography in benign and malignant thoracic lesions. *Nucl Med Commun* 1993;14:1071-8
7. Chin BB, Zukerberg BW, Buchpiguel C, Alavi A. Thallium-201 uptake in lung

- cancer. *J Nucl Med* 1995;36:1514-9
8. Yamamoto Y, Nishiyama Y, Fukunaga K, Satoh K, Ohkawa M. Tl-201 chloride and Tc-99m MIBI accumulation in lung adenocarcinoma in patients with and without distant metastases. *Clin Nucl Med* 2001;26:751-6
 9. Vertosick FT Jr, Selker RG, Grossman SJ, Joyce JM. Correlation of thallium-201 single photon emission tomography and survival after treatment failure in patients with glioblastoma multiforme. *Neurosurgery* 1994;34:396-401
 10. Elgazzar AH, Fernandez-Ulloa M, Silberstein EB. ²⁰¹Tl as a tumour-localizing agent : current status and future considerations. *Nucl Med Comm* 1993;14:96-103
 11. Kahn D, Follet KA, Bushnell DA, et al. Diagnosis of recurrent brain tumor : value of ²⁰¹Tl SPECT vs ¹⁸F-fluorodeoxyglucose PET. *Am J Roentgenol* 1994;163:1459-65
 12. Pennes DR, Glazer GM, Wimbish KJ, Gross BH, Long RW, Orringer MB. Chest wall invasion by lung cancer: limitations of CT evaluation. *Am J Roentgenol* 1985;144:507-11
 13. Vansteenkiste JF, Stroobants SG, Kuriyama K, Tateishi R, Kumatani T, et al. Pleural invasion by peripheral bronchogenic carcinoma: assessment with three-dimensional helical CT. *Radiology* 1994;191:365-9
 14. Erasmus JJ, Patz EF. Positron emission tomography imaging in the thorax. *Clin Chest Med* 1999;20:715-24
 15. Kim EE, Chung SK, Haynie TP, et al. Differentiation of residual or recurrent tumors from post-treatment changes with F-18 FDG-PET. *Radiographics* 1992;12:269-79
 16. Abdel-Dayem H, Bag R, Macapinlac H, Elgazzar AH, Habbab N, Pescatore F, et al. Diffuse Tl-201 uptake in the lungs: etiologic classification and pattern recognition. *Clin Nucl Med* 1995;20:164-72
-