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# On the Diagnostic Imaging of Solitary Pulmonary Nodule (SPN)

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**Abstract** The difference in $^{201}$TI-choride ($^{201}$TI) accumulation on single photon emission computed tomography (SPECT) between 58 benign (58 cases) and 48 malignant (46 cases) thoracic lesions, each of more than 20mm in diameter was investigated. In the 34 benign and 48 malignant lesions depicted in both early (15min) and delayed (3h) images there was no significant difference in the mean early and delayed uptake ratios of lesion to normal contralateral lung between benign and malignant. However, the retention index in the lesion derived from (delayed ratio-early ratio)/early ratio $\times 100\%$ showed a significant difference (benign $-4.30 \pm 18.9\%$, $P < 0.01$) indicating the poor $^{201}$TI retention in the benign lesions. Using the criteria of nondepiction in the delayed image or a negative retention index, 81.1% accuracy and 95.2% predictive value for diagnosis of benign lesions were obtained. Thus, $^{201}$TI SPECT appears to have potential usefulness in the diagnosis of benign thoracic lesions.

*Key Words* : Thalium 201, SPECT, Lung cancer, Benign lesion, Malignant lesion

## Introduction

The diagnosis of solitary pulmonary nodule (SPN) on chest radiograph was very difficul t in differentiation from benignity and malignancy.

They (SPN) may be more accurately diagnosed by computed tomography (CT) than conventional tomography, because of the superior contrast resolution of CT.

Especially, using the high-spatial frequency reconstruction algorithm and thin -section scanning, high resolution CT (HRCT) is very useful to obtain the image of the lung parenchyma.

We have described on the comparison of HRCT image of the features of small peripheral type lung cancer surgically resected, already. (Yamaguchi Medical Journal, 43, 1-9, 1994) and so, would describe on the nuclear techinical diagnosis of SPN,; I Differentiation of $^{201}$TI accumulation on single photon emission computed tomography in benign and malignant thoracic lesions. Additionally, the mass survey of lung cancer with computerized nodule detection in screening for lung cancer; II Potential usefulness of computed nodule detection in screening program.

## I Difference in $^{201}$TI accumulation on single photon emission computed tomography in benign and malignant thoracic lesions

### Introduction

$^{201}$TI-chloride ($^{201}$TI) scintigraphy has been widely used to detect various tumors and the recent use of single photon emission computed tomography (SPECT) has im-

proved the depicition of thoracic tumors compared to planner images (1), providing additional information to the morphological data by X-ray CT in patients with primary lung cancers, metastatic hilar or mediastinal lymph nodes and mediastinal tumors (1-4). On the other hand, $^{201}$TI accumulates not only in malignant tumors but also in inflammatory lesions and benign tumors (5, 6). However, previous animal and several clinical investigations have indicated that $^{201}$TI has more prolonged retention in malignant tumors than benign lesions (5-8). However, as far as thoracic lesions are concerned, few investigations have studied the difference between $^{201}$TI accumulation in malignat and benign lesions. The present syudy using $^{201}$TI SPECT was conducted to investigate this difference (9).

## Subject and methods

A total of 106 thoracic lesions (in 104 cases) due to various benign conditions and malignant lesions were studied at our institution between February 1990 and January 1993. We studied all patients with lesions larger than 20 mm in diameter. Moreever, lesions adjacent to the myocardium were excluded from this study in order to avoid the influence of Compton scattering from the $^{201}$TI actvity in the myocardium.

There were 58 benign lesions (58 cases) and 48 malignant lesions (46 cases) (Table 1) from 70 men and 34 women ranging 39 to 85 years (mean 67.8 years; median 65 years). All patients underwent chest radiography and CT 3-12 days before $^{201}$TI SPECT.

### $^{201}$TI SPECT

After intravenous injection of 166.5-222 MBq $^{201}$TI, tomographic scans were performed at 15 min (early images) and 3h (delayed images) using a rotating gamma camera system with a single head, equipped with a high-resolution collimetor (Toshiba GCA 901-A, Japan). A one-peak energy window (80 Kev) was used.

Sixty projections obtained with an acquisition time of 20s each were stored.

The filterd backprojection method was employed for image reconstruction using a Ramachandran-Logan filter to suppress high -frequency noise. Subsequently, transverse sections were reconstructed. Attenuation correction was not performed. When $^{201}$TI SPECT showed abnormal accumulation in the lesions, quantitative analysis by setting regions of interst (ROIs) was performed as follows.

Table 1 : Summary of Lesions

| Benign disorders | | Malignant tumors | |
|---|---|---|---|
| Pulmonary tuberculosis (Active 10, Inactive 6) | 16 | Primary lung cancer (Adeno. 14, Squamous. 7, Small. 2, Adenosquamous. 1, Undifferentiated ca. 1) | 25 |
| Active pneumonia | 9 | | |
| Silicosis | 6 | | |
| Radiation pneumonitis | 6 | Metastatic lymph node (Hilar: Adeno. 2, Small. 2, Squamous. 1, Mediastinal; Adeno. 2, Squamous. 1, Plasmocytoma 1) | 9 |
| Atypical mycobacterial disease | 4 | | |
| Chronic empyema | 4 | | |
| Organizing pneumonia | 4 | | |
| Inflammatory pseudotumor | 2 | | |
| Aspergilloma | 2 | Metastatic lung tumor (Lung 2, Gallbladder 2, Urinary bladder 1, Rectum 1, Thyroid 1) | 7 |
| Bronchogenic cyst | 2 | | |
| Granulloma | 2 | | |
| Mediastinal tumor | 1 | | |
| | | Malignant lymphoma | 3 |
| | | Lung tumor of unknown histology | 3 |
| | | Mesothelioma | 1 |
| Total | 58 | | 48 |

Adeno; Adenocarcinoma, Squamous; Squamous cell carcinoma,
Small; Small cell carcinoma, ca; carcinoma

### Early and delayed uptake ratios

To assess the degree of $^{201}$ uptake in the lesions, ROIs were set over the areas of abnormal radioactivity and in the corresponding site of the contralateral normal lung on transverse sections of both early and delayed images.

The mean voxel counts of the ROIs were measured and the uptake ratio of the lesion to contralateral normal lung was caluculated for both images. The transverse planes which demonstrated the lesion most clearly were carefully selected, and the identical positions of the ROIs in the lesion in both images were carefully confirmed.

### Retention Index

Absolute quantification is diffucult with SPECT to evaluate the previously reported observation that benign lesions showed significant decrease in $^{201}$TI activity over time whereas malignant lesions retain or further accumulate activity over time (5-7). Therefore, we used the relative index of the lesion to control area in the contralateral lung, and when the lesion was depicted in both early and delayed images, the retention index was calculated to evaluate $^{201}$TI retenton in the lesions as follows:

$$\frac{\text{Delayed uptake ratio-Early uptake ratio}}{\text{Early uptake ratio}} \times 100\% \quad (1)$$

Thus, the formula was looking at the most simple mathematical expression of the relative change of $^{201}$TI uptake in the lesions over time normalized to a control area. Statistical analysis performed using Student's t-test to determine the significance of differences between the mean values of the early ratio, the delayed ratio and the retention index. Difference were considered significant at $P < 0.05$.

## Results

On the early $^{201}$TI SPECT images, 39 (67.2%) of the 58 benign disorders and all of the 48 malignant lesions were positive. On the planner $^{201}$ Tl image, 24 (41.3%) of the 58 benign disorders and 34 (70.8%) of the 48 malignant lesions were positive, and all of these positive lesions were depicted on the $^{201}$ TI SPECT images. Of the total 87 lesions depicted on the early $^{201}$ TI SPECT images, five benign lesions were not depicted on the delayed images.

For the 34 benign lesions and 48 malignant lesions depicted on both images, the mean early uptake ratio was $1.9 \pm 0.4$ for benign lesions and $2.1 \pm 0.7$ for malignat lesions, with no significant difference (N.S.). The mean delayed uptake ratio was $1.7 \pm 0.4$ for benign lesions and $2.5 \pm 1.0$ for malignant lesions, and again there was no significant difference. However, retention index was $-4.3 \pm 13.6\%$ for benign lesions and $23.3 \pm 18.9\%$ for malignant lesions, showing a significant difference ($P < 0.01$) (Fig. 1). Two patients with a malignant or benign lesion, which showed a typical pattern of $^{201}$ TI accumulation, are shown in Fig 2 and 3.

Of 23 lesions with a negative retention index, 21 lesions were benign and only two lesions were malignant. One of the two malignat lesions, which showed a negative retention index value, was an alveolar cell carcinoma of 28 mm, whose histology revealed massive mucus deposits around the tumour. The other malignant lesion with a negative value was a mediastinal (subcarinal) metastatic lymph node from lung cancer of adenocarcinoma, measuring 25 mm in diameter.

Overall, when lesions not depicted in the delayed image or showing negative values of retention index were defined as benign, the accuracy was 81.1%, the predictive value for a benign lsione was 95.2%, the sensitivity for a benign lesion was 69.0%, and the specificity for a benign lesion was 95.8%.

Two patients in whom $^{201}$ TI SPECT showed the characteristic patterns of the lesions better than chest radiography or CT.

## Discussion

The present results indicate that the bening lesions have a tendency to be negative for $^{201}$ TI accumulation despite their relatively large

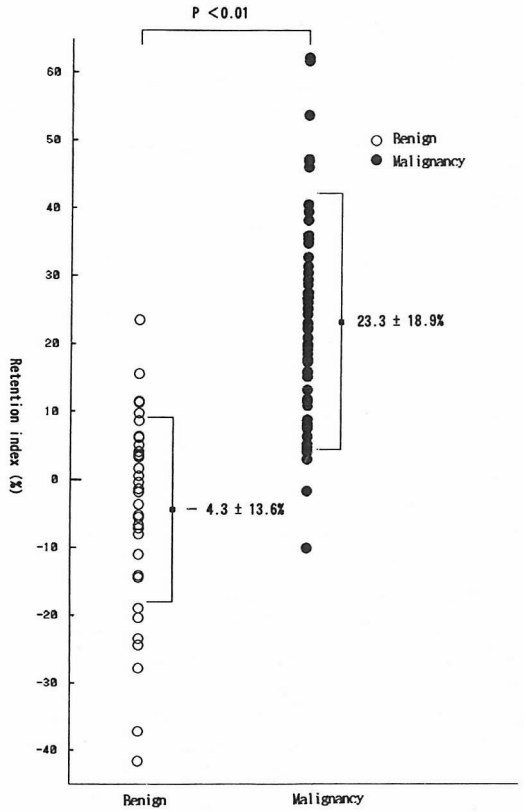
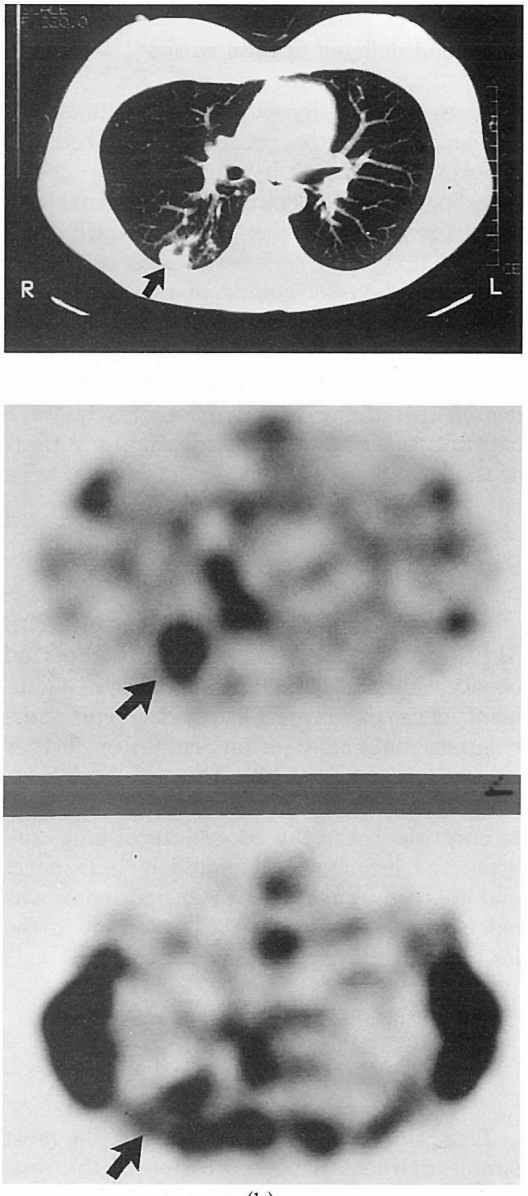


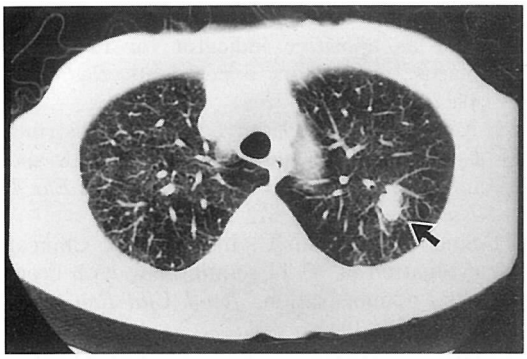

Fig. 1 Comparison of retention index between benign and malignant lesions.
The retention index was −4.3±13.6% for benign lesions and 223.3±18.9%, for malignant lesions, showing a significant difference ($p<0.01$). Of the 23 lesions with a negative value of retention index, were benign and only two were malignant.

size, and that malignant lesions tend to be positively depicted more frequently than benign lesions. Previous studies have also demonstrated the same tendency in extrathoracic lesions (5,8,10). However, our results demonstrated that both the early and delayed lesion to normal lung ratios of the benign had no significant difference from the malignant lesions. This findings is different from that obtained in the previous study by Tonami et al. (2) which was performed using high-dose admulnistrated of $^{201}$ TI (296-370 MBa) in 23 patients with lung cancer and seven with various benign thoracic lesions.

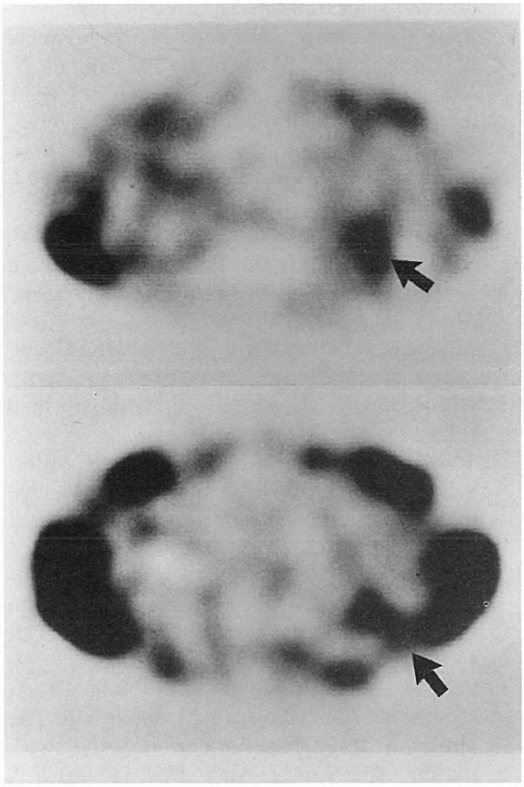



(b)

Fig. 2 A 21-years-old patient with active pulmonary tuberclosis.
a) Chest computed tomography showing abnormal density in the right lung (arrow).
b) TI SPECT demonstrated accumulation in the early image; however, the accumulation was decreased visually on the delayed image (arrow). The early and delayed uptake were 1.65 and 1.42, respectively.
The retention index was −13.9%.



(a)



(b)

Fig. 3 A 62-year-old patient with lung cancer (adenocarcinoma).
a) Chest computed tomography showing a nodular lesion in the left upper lung.
b) TI SPECT showing accumulation corresponding to the lesion on both early and delayed ratios were 1.35 and 1.57, respectively. The retention ingex was 16.3%.

On the other hand, previous investigators have indicated that $^{201}$ TI has more prolonged retention by malignant tumors than benign lesions. Ando et al. (6) showed that $^{201}$ TI also accumulated in inflanmatory lesions and that its uptake decreased with time, but that $^{201}$ TI washout from malignant tumours tend to be delayed. Sindo et al. (7) reported that $^{201}$ TI showed delayed washout from lung cancers compared to benign pulmonary lesions in scintigraphy using $^{201}$ TI administered via the the bronchial artery. Ochi et al. (8) reported more delayed washout of $^{201}$ TI from malignant thyroid tumors compared with benign ones. Therefore, we tried to quantify these previously reported observations with $^{201}$ TI SPECT (9).

Sodium-potassium pump (Na+ − K+ ATPase) activity and tumour blood flow are the main mechanisms of $^{201}$ TI uptake by tumours (10-13). In lung cancers, Sehweil et al. (14) reported that the time from injection of $^{201}$ TI to peak tumour activity was 11.9 min, followed by gradual washout and loss of about 25% of activity during the 4 h after injection. On the other hand, the normal lung activity of $^{201}$ TI decreased rapidly to nearly reach a plateau level whithin 100-150 s after injection, after which slight and gradual decrease continued for 30 min (15). The early and delayed ratios obtained in our study are determined by the difference in the degree of $^{201}$ TI retention by the lesions and the normal lung. Therefore, we can quantify relative changes in lesion count rates over time by the formula exhibited (the retention index). As a result, the average retention index showed a signifficant difference, with the benign lesions having lower values than the malignant lesions. This supports the previous observations that benign thoracic lesions show a significant decrease in $^{201}$ TI activity over time, wheares malignant lesions retain or further accumulate activity over time. Among the 23 lesions with negative retention index value, there were only two malignant lesions (8.6%). One was an alveolar cell carcinoma of 28 mm, which histologically showed massive mucus deposits aruond the tumour, and it was thus speculated that this exceptional value of the retention index was caused by the tumour size being smaller than

the size resolveable by CT due to the surrounding mucus. The other malignant lesion with a negative value was a sub carinal metastatic lymph node (adenocarcinoma), in which it was speculated that because the lesion was located deeply the delayed uptake ratio might be underestimated due to photon attenuation.

In conclusion, the results of this preliminary study using SPECT apparatus with a single headed detector rotating system indicate that benign thoracic lesions tend to be not depicted or to show more rapid washout of $^{201}$ TI compared to malignat lesions. The sensivility and system resolution of our instrumentation are inferior to those of newer equipment such as the three headed rotating system. However, our results of 81.1% accuracy and 95.2% predictive value for diagnosis of benign lesions, using the criteria of nondepiction in delayed image or a negative retention index, are relatively good. Thus, $^{201}$ TI SPECT appears to have potential usefulness in diagnosis of benign thoracic lesions.

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