

## Favorable biodistribution of $^{99m}\text{Tc}$ -ECD for brain SPECT comparing with $^{123}\text{I}$ -IMP using alternative body scan

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In order to evaluate the lung and brain uptake of  $^{99m}\text{Tc}$  ethyl cysteinate dimer ( $^{99m}\text{Tc}$ -ECD) and N-isopropyl-p-[ $^{123}\text{I}$ ]-iodoamphetamine ( $^{123}\text{I}$ -IMP), alternative body scans were carried out in 15 cases of cerebrovascular disease. The biodistribution of  $^{99m}\text{Tc}$ -ECD was  $5.5 \pm 0.7\%$ ,  $3.8 \pm 0.7\%$  in the brain;  $13.1 \pm 3.7\%$ ,  $2.2 \pm 1.2\%$ , in the lung at 15 min and at 4 hours, respectively, whereas that of  $^{123}\text{I}$ -IMP was  $3.9 \pm 1.4\%$ ,  $5.0 \pm 1.0\%$  in the brain;  $32.2 \pm 7.6\%$ ,  $12.7 \pm 3.3\%$ , in the lung at 15 min and at 4 hours, respectively.  $^{99m}\text{Tc}$ -ECD accumulated in comparatively high amounts in the brain but remained low in the lung in the early image compared to  $^{123}\text{I}$ -IMP. However there was a high inverse correlation between brain and lung uptake of  $^{123}\text{I}$ -IMP ( $r = -0.82$ ), but not of  $^{99m}\text{Tc}$ -ECD ( $r = -0.18$ ).

We concluded that  $^{99m}\text{Tc}$ -ECD had a better biodistribution in terms of low lung accumulation than  $^{123}\text{I}$ -IMP in brain SPECT.

**Key words:**  $^{99m}\text{Tc}$ -ECD,  $^{123}\text{I}$ -IMP, lung uptake, brain uptake

### INTRODUCTION

TECHNETIUM-99m ethyl cysteinate dimer ( $^{99m}\text{Tc}$ -ECD) accumulates in the brain parenchyma by rapid deesterification to a polar metabolite which does not recross the blood brain barrier.<sup>1-3</sup> N-isopropyl-p-[ $^{123}\text{I}$ ]-iodoamphetamine ( $^{123}\text{I}$ -IMP) indicates regional cerebral blood flow,<sup>4-7</sup> but it may tend to be trapped in the pulmonary endothelium,<sup>8</sup> and then cannot reach the brain effectively.

The aim of this study is to evaluate lung and brain accumulation of  $^{99m}\text{Tc}$ -ECD and  $^{123}\text{I}$ -IMP in analyzing the biodistribution by alternative body scans which are made up of multiple body images so as to calculate the organ uptake rate even in patients with cerebrovascular disease.

### MATERIALS AND METHODS

After informed consent had been obtained, 15 pa-

tients (male/female = 14/1,  $66 \pm 10$  yr), who were diagnosed as having cerebrovascular disease, were subjected to  $^{99m}\text{Tc}$ -ECD and  $^{123}\text{I}$ -IMP brain SPECT within one week to evaluate the clinical usefulness of the radiopharmaceuticals in biodistribution. Ten of 15 patients were heavy smokers (more than 20 cigarettes per day over 20 years), and 4 patients showed signs of impaired renal function (more than 20 mg/dl in blood urea nitrogen).

#### *Preparation of the radiopharmaceuticals*

$^{99m}\text{Tc}$ -ECD was prepared from two vials: vial A (ECD 2HCl 0.90 mg,  $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$  0.072 mg,  $\text{Na}_2\text{EDTA} \cdot 2\text{H}_2\text{O}$  0.36 mg, mannitol 24.0 mg), and vial B ( $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$  0.460 mg,  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$  4.105 mg, purified water 1 ml) (DuPont Company No. Billerica, MA). Saline (3 ml) was injected into vial A to dissolve its content. After 30-45 mCi (1,110-1,665 MBq) of  $^{99m}\text{Tc}$  pertechnetate, which was eluted within 48 hours after the previous elution, was injected into vial B, one ml of the contents of vial A was then transferred into vial B. The mixture was allowed to stand at room temperature for 30 min. The radiochemical purity of the final solution was determined by thin layer chromatography. The radiochemical purity of  $^{99m}\text{Tc}$ -ECD by chro-

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matography. The radiochemical purity of  $^{99m}\text{Tc}$ -ECD by chromatography was  $97.7 \pm 0.4\%$  in 8 of 15 cases. 15 mCi (555 MBq) of  $^{99m}\text{Tc}$ -ECD was then injected. 4.5 mCi (166.5 MBq) of  $^{123}\text{I}$ -IMP (Nihon Medipysics Co.) was prepared by the  $^{127}\text{I}(\text{p},5\text{n})^{123}\text{Xe} \rightarrow ^{123}\text{I}$  reaction with less than 4.5% of  $^{125}\text{I}$  contamination at the time of injection.

#### *Biodistribution by alternative body scan*

The radiopharmaceutical was administered intravenously in a supine patient with the eyes closed by a mask for 15 min before and after injection. Prior to brain SPECT in order to evaluate biodistribution, alternative body scans were taken in the following sequence: posterior abdomen, anterior pelvis, anterior abdomen, anterior chest and anterior head for one minute collection at 15 min (early image) and 4 hours (delayed image) after the injection of the radiopharmaceutical. A conventional gamma camera (General Electric Co., Starcam 400AC/T) equipped with a general all purpose collimator for  $^{123}\text{I}$ -IMP and with a high resolution collimator for  $^{99m}\text{Tc}$ -ECD was used. The brain and lung counts were derived from the region of interest of the brain and the lungs on the anterior head and anterior chest of alternative body scans. Then, the liver and kidney counts were obtained as the average counts from the regions of interest of the liver and kidneys on the anterior and posterior abdominal alternative body scans. Whole body counts (=WBC) in the early image were also obtained as the summation of the territory counts in the anterior head, anterior chest, anterior pelvis and averaged abdomen without overlapping these images (Fig. 1). For sequential semi-quantitative analysis, counts for the brain, lungs, liver and kidneys were obtained in both early and delayed images, then WBC in the delayed image was obtained from that in the early image after correction for physical decay. The uptake ratio of an organ to that for the whole body in the early image [=UPTAKE(e)] were obtained with equation (1) and that in the delayed image [=UPTAKE(d)] with equation (2).

$$\text{UPTAKE(e)} = \frac{\text{counts in an organ}}{\text{WBC in the early image}} \quad (1)$$

$$\text{UPTAKE(d)} = \frac{\text{counts in an organ}}{\text{WBC}^* \text{ in the early image}} \quad (2)$$

(\*: corrected for physical decay)

#### *Brain SPECT*

Brain SPECT was carried out with a conventional single rotating gamma camera as alternative body scan. Data were obtained from 64 projections into a  $64 \times 64$  matrix, using a general all purpose collimator for  $^{123}\text{I}$ -IMP and a high resolution collimator for  $^{99m}\text{Tc}$ -ECD. The sampling time for both  $^{99m}\text{Tc}$ -ECD brain SPECT and  $^{123}\text{I}$ -IMP brain SPECT was 20 sec. Data collection for the early brain SPECT was started 30 min after the radiopharmaceutical was injected. All data were corrected for an attenuation of  $0.1 \text{ cm}^{-1}$  and the tomographic data were reconstructed by means of a filtered back-projection algorithm. Based on the lead bar generated orbitomeatal line from the right lateral planar image using the mark on the right eye and the right external meatus prior to SPECT. The sliced planes of the transaxial section were determined. The slice of each section was 6 mm in thickness. All results were expressed as the mean  $\pm$  standard deviation. The significance of difference was calculated by paired t-test to obtain the early/delayed images and the unpaired t-test to obtain the  $^{99m}\text{Tc}$ -ECD/ $^{123}\text{I}$ -IMP ratio images. A p value of less than 0.05 was considered to be significant.

## RESULTS

#### *Biodistribution by alternative body scan*

Comparing the early image with the delayed image, the uptake ratio of  $^{99m}\text{Tc}$ -ECD was changed from  $5.5 \pm 0.7\%$  to  $3.8 \pm 0.7\%$  ( $p < 0.01$ ) in the brain,  $13.1 \pm 3.7\%$  to  $2.2 \pm 1.2\%$  ( $p < 0.01$ ) in the lungs,  $9.6 \pm 2.6\%$  to  $1.3 \pm 0.4\%$  ( $p < 0.01$ ) in the liver and  $7.6 \pm 2.2\%$  to  $1.0 \pm 0.4\%$  ( $p < 0.01$ ) in the kidneys, whereas that of  $^{123}\text{I}$ -IMP was changed from  $3.9 \pm$

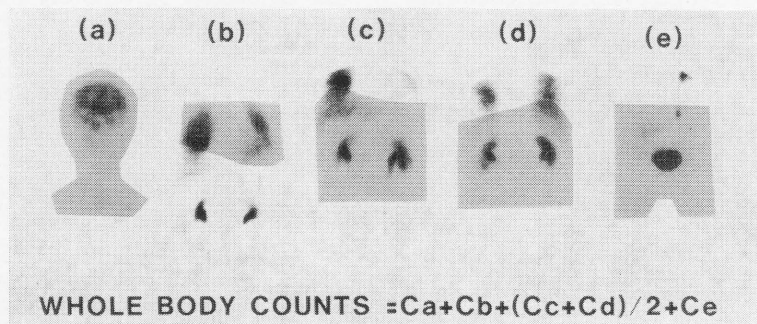
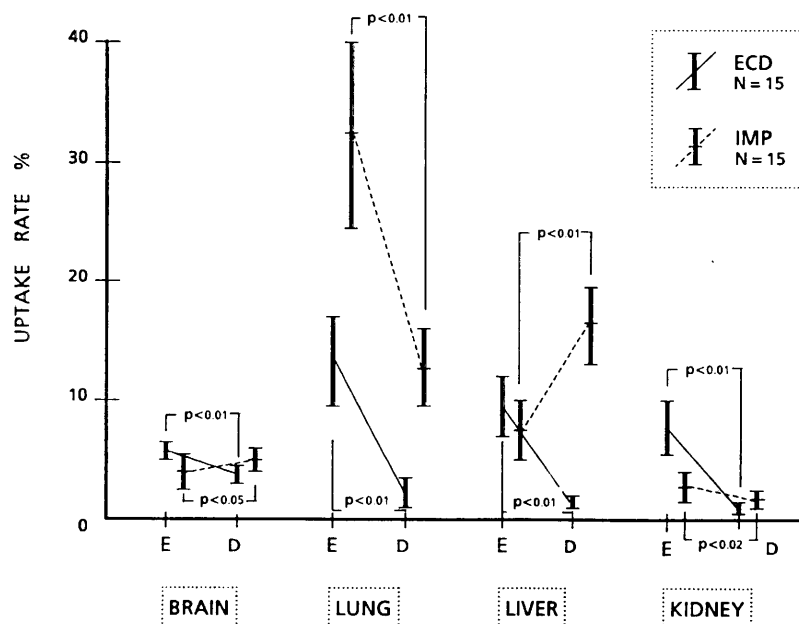
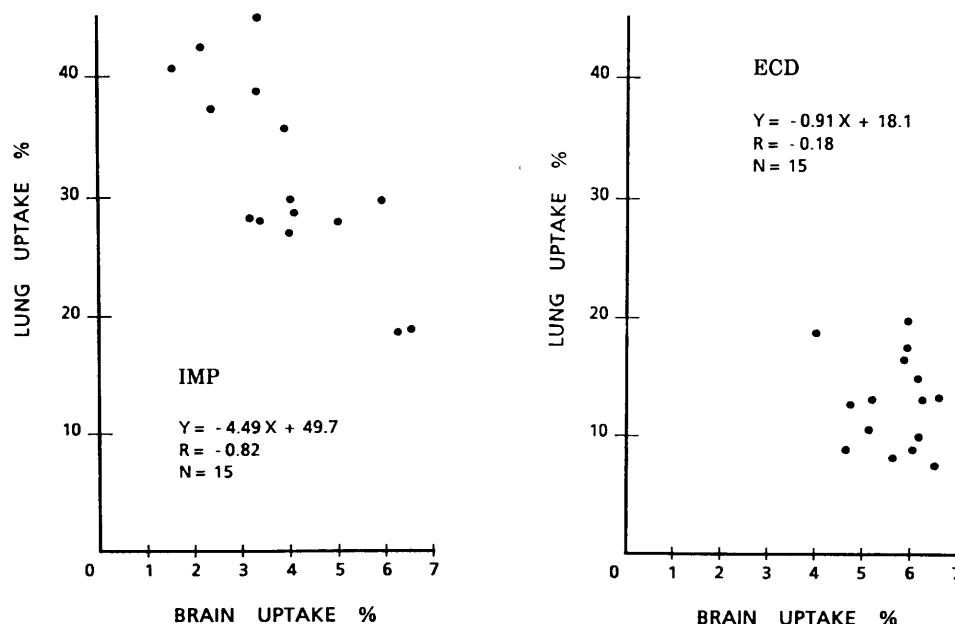


Fig. 1 Alternative body images to assess biodistribution.



**Fig. 2** Biodistribution of  $^{123}\text{I}$ -IMP and  $^{99\text{m}}\text{Tc}$ -ECD by alternative body scan. E=Early biodistribution, D=Delayed biodistribution.



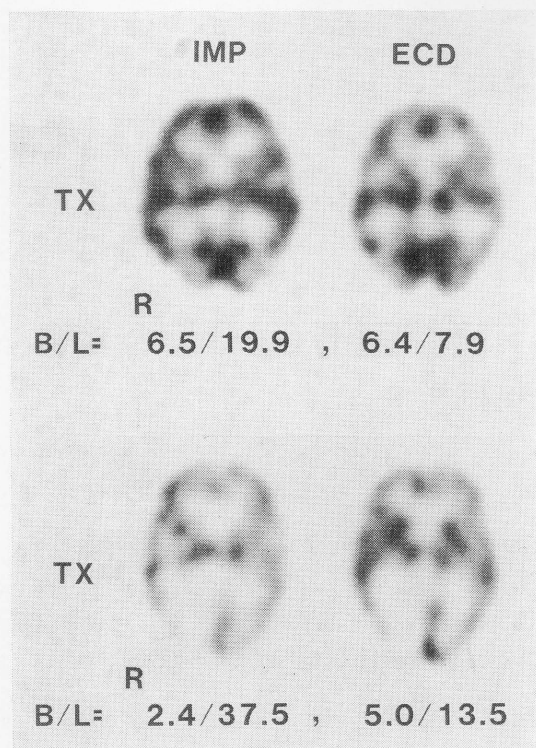
**Fig. 3** Correlation between lung and brain uptakes in  $^{123}\text{I}$ -IMP and  $^{99\text{m}}\text{Tc}$ -ECD alternative scans in the early image. IMP= $^{123}\text{I}$ -IMP, ECD= $^{99\text{m}}\text{Tc}$ -ECD.

1.4% to  $5.0 \pm 1.0\%$  ( $p < 0.05$ ) in the brain,  $32.2 \pm 7.6\%$  to  $12.7 \pm 3.3\%$  ( $p < 0.01$ ) in the lung,  $7.9 \pm 2.9\%$  to  $16.2 \pm 3.3\%$  ( $p < 0.01$ ) in the liver and  $2.8 \pm 1.3\%$  to  $1.8 \pm 0.6\%$  ( $p < 0.02$ ) in the kidneys (Fig. 2). Comparing  $^{99\text{m}}\text{Tc}$ -ECD with  $^{123}\text{I}$ -IMP, the uptake ratio at 15 min was significantly ( $p < 0.01$ ) higher in the brain and lower in the lung. The lung uptake ratio of heavy smokers ( $35.5 \pm 6.8\%$ ,  $n = 10$ ) in the early biodistribution of  $^{123}\text{I}$ -IMP was significantly ( $p < 0.05$ ) higher than that of light smokers or non-

smokers ( $25.7 \pm 5.7\%$ ,  $n = 5$ ), but the lung uptake ratio of  $^{99\text{m}}\text{Tc}$ -ECD in those who were having impaired renal function ( $5.7 \pm 0.8\%$ ,  $n = 4$ ) was not significantly higher than those who had normal renal function ( $5.47 \pm 0.7\%$ ,  $n = 11$ ).

#### *Comparison of brain and lung uptake in the early image*

There was a high inverse correlation between lung uptake (=Y) and brain uptake (=X) of  $^{123}\text{I}$ -IMP



**Fig. 4**  $^{123}\text{I}$ -IMP brain SPECT uptake is equivalent in image quality to  $^{99\text{m}}\text{Tc}$ -ECD brain SPECT (Upper row).  $^{123}\text{I}$ -IMP brain SPECT is inferior to  $^{99\text{m}}\text{Tc}$ -ECD brain SPECT because of high lung accumulation (Lower row). R=Right, TX=Transaxial section, B=Brain uptake rate, L=Lung uptake rate, other abbreviations as in Fig. 3.

with the equation  $Y = -4.49X + 49.7$ ,  $r = -0.82$ , but there was no correlation between those of  $^{99\text{m}}\text{Tc}$ -ECD ( $r = -0.18$ ) (Fig. 3).

Two cases were shown for comparison. A case of high brain and low lung uptake by biodistribution with  $^{123}\text{I}$ -IMP was equivalent in image quality to  $^{99\text{m}}\text{Tc}$ -ECD. However, a case of low brain and high lung uptake by biodistribution with  $^{123}\text{I}$ -IMP brain SPECT was apparently inferior to that with  $^{99\text{m}}\text{Tc}$ -ECD after reconstructing the brain SPECT image (Fig. 4).

### DISCUSSION

Alternative body scan was first done with  $^{99\text{m}}\text{Tc}$ -HM-PAO<sup>9</sup> and was easily done in less than ten minutes even in patients with cerebrovascular disease to see the relative biodistribution. The biodistribution of  $^{99\text{m}}\text{Tc}$ -ECD in alternative body scan showed rapid washout from the lung and the liver and excretion from the urinary system, and that of  $^{123}\text{I}$ -IMP showed high accumulation in the lung in the early image and increased activity in the liver and the brain in the delayed image due probably to the

accumulation of  $^{123}\text{I}$ -IMP metabolite.<sup>10</sup> The uptake rate in alternative body scan was relatively in accord with that in the single pass method with  $^{123}\text{I}$ -IMP<sup>10</sup> and  $^{99\text{m}}\text{Tc}$ -ECD,<sup>11</sup> respectively.

At the first extraction, less affinity with the lung is important for brain perfusion agents in order to accumulate in the brain to express cerebral blood flow effectively.  $^{123}\text{I}$ -IMP indicated significantly high affinity with the lung compared to  $^{99\text{m}}\text{Tc}$ -ECD in patients who were heavy smokers.<sup>12</sup>  $^{123}\text{I}$ -IMP brain SPECT with high lung accumulation might provide poor image quality in patients who are heavy smokers habit, whereas  $^{99\text{m}}\text{Tc}$ -ECD brain SPECT displayed consistently excellent brain SPECT images which were not affected by the lung accumulation of  $^{99\text{m}}\text{Tc}$ -ECD in patients even with impaired renal function. In selecting the collimator, it was preferable to use a high resolution collimator when measuring the distribution of cerebral blood flow accurately<sup>13</sup> instead of a general all purpose collimator which has twice the counting sensitivity at the expense of resolution for  $^{99\text{m}}\text{Tc}$  and for  $^{123}\text{I}$ . But we have to use a general all purpose collimator with  $^{123}\text{I}$ -IMP to get enough counts for brain SPECT with a single rotating gamma camera within twenty minutes for acquisition.  $^{99\text{m}}\text{Tc}$ -ECD could not only be injected over three time dose of  $^{123}\text{I}$ -IMP in view of equivalent radiation hazard but also showed less affinity with the lung, resulting in higher accumulation in the brain than  $^{123}\text{I}$ -IMP.

We concluded that  $^{99\text{m}}\text{Tc}$ -ECD had a better biodistribution in terms of low lung accumulation than  $^{123}\text{I}$ -IMP for brain SPECT.

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