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Early and delayed imaging with ^{123}I-IMP SPECT in patients with ischemic cerebrovascular disease

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Cerebral blood flow imaging with N-isopropyl (I-123) p-iodoamphetamine (IMP) was performed in 44 patients with ischemic cerebrovascular disease (CVD) at an acute or subacute stage less than 30 days from the onset. IMP imaging was obtained at 20 minutes (early scan) and 4 hours (delayed scan) after intravenous injection of 222 MBq of IMP. The region of interest (ROI) was selected in a slice compatible with the findings on the CT images, and the lesion to tissue ratio (L/T ratio) was calculated in a comparison with the unaffected side. The redistribution index (RI) was also calculated by dividing the difference between the L/T ratio in early and delayed image by the L/T ratio in early image. The patients were classified into three groups (Grade 1, 2, 3) on the basis of the CT findings. The L/T ratio in the delayed images and RI was high in grade 1 and 2 groups and low in grade 3 groups both in early and delayed scans. The RI had tendency to grow high as the days after the onset became later. In the duration period from 4 to 7 days, 'reversed' redistribution was observed in 4 cases. Follow up examinations were performed in 6 cases in grade 3 group. The RI became higher in 3 cases and lower in 3 cases in the second examination.

In conclusion, good redistribution was observed in grade 1 and 2 groups, and the prognosis was good. On the other hand, poor redistribution was observed in grade 3 group. There was little relationship in the degrees of redistributions or 'reversed' redistribution between the first and second examination in grade 3 group.

Key words: ^{123}I-IMP SPECT, Cerebrovascular disease, Cerebral blood flow, Reversed redistribution, Redistribution

INTRODUCTION

IMP is a radiopharmaceutical used for imaging regional cerebral blood flow (rCBF). It is widely used for imaging rCBF in various cerebral diseases, because IMP SPECT image at early stage after intravenous injection of IMP is proportional to regional cerebral blood flow in normal subjects and those with cerebrovascular disease.[1,2] However, the distribution of IMP changes with time. Redistribution or 'filling in' phenomena were observed in the delayed IMP SPECT images in the ischemic area.[3] Therefore, a delayed IMP image may give useful information concerning the viability of ischemic brain tissue.[4]

In this paper, the relationship between redistribution and the grade of CT was reported.

MATERIALS AND METHODS

Forty-four patients were selected when clinical or X-ray computed tomography (CT) showed that they had ischemic cerebrovascular disease (CVD). They include 6 cases with transient ischemic attacks (TIA) and 38 cases with cerebral infarction. The length of

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time between the IMP study and the onset was between 1 day and 30 days.

On the basis of the CT findings, the patients were classified in to three groups. Grade 1 (6 cases); no low density area, Grade 2 (15 cases); low density area smaller than 2 cm in diameter, and Grade 3 (23 cases); low density area larger than 2 cm in diameter. CT was performed within 2 days from the IMP study. All were subjected to follow up examinations by CT within 1 month, which showed the same grades. In grade 3 group, follow up examinations were performed in 6 cases at a few weeks after the first examination. Table 1 shows the age and sex distribution in the 3 groups. They did not differ significantly in the 3 groups in t-test and χ^2-test ($p>0.01$).

Each patient received 222 MBq (6 mCi) of ^{123}I-IMP. The imaging was begun 20 minutes (early scan) and 4 hours (delayed scan) after the injection, using a 35×50 cm large field rotating scintillation camera (GCA-90A), Toshiba Medical Co., Ltd.) equipped with a low energy high resolution parallel hole collimator with a 20% window centered over the 159 keV ^{123}I photopeak. The SPECT acquisition was undertaken in 60 steps and each step acquired counts through 30 sec. Data were collected in 128×128 matrices and stored on the memory disk of a computer (GMS-55U, Toshiba Medical Co., Ltd.). From these 128×128 matrices the computer could reconstruct transverse sections with filtered back projection and a Shepp and Logan filter was used without attenuation or scatter correction. SPECT images were obtained between the top of the cortex and the lower edge of the cerebellum chosen by the operator with depth of 4 pixels (12 mm).

Regions of interest (ROIs) were set in a compatible slice of SPECT images obtained by IMP. A circle ROI (ROI1) in diameter of 7 pixels (21 mm) was set in the center of the affected region observed on CT image. The same sized ROI (ROI2) was also set in the symmetrical region on the opposite side. The lesion to tissue ratio (L/T ratio) was obtained by dividing the counts of ROI1 by those of ROI2. The redistribution index (RI) was calculated by dividing the difference between the L/T ratios in early and delayed images by that in early image.

Table 1 Age and sex distribution in 3 groups

CT	Male	Female	Age (±S.D.)
Grade I	2	4	63.0± 9.0
Grade II	8	7	66.5±11.1
Grade III	10	13	71.9±11.0
Total	20 (Cases)	24	68.1±12.0 (Years)

RESULTS

The L/T ratios for each CT grade are shown in Figure 1. In grade 1, the mean±s.d. was 96.3±2.1 in the early image and 100.6±2.7 in the delayed image. In grade 2, the mean±s.d. was 92.5±8.3 in the early image and 97.4±7.2 in the delayed image. In grade 3, the mean±s.d. was 73.0±22.7 in the early image and 77.2±24.0 in the delayed image. Good redistribution was observed in grades 1 and 2, and the prognosis was also good in these groups. However, the L/T ratios were low in early and delayed images in the grade 3 group.

The RIs according to duration after the onset in grade 3 cases are shown in Figure 2. The RIs have a tendency to become high with time after the onset. In the period from 4 days to 7 days, the values varied from −20.1 to +16.0 and those showed minus values

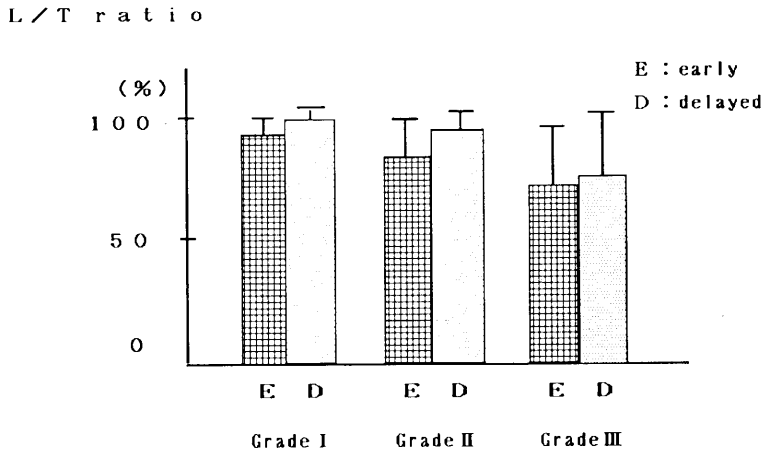

Fig. 1 L/T ratios for each CT grade. E; early image, D; delayed image. Good redistribution was observed in grades 1 and 2. The L/T ratio was low in grade 3 and standard deviation was large in early and delayed images.

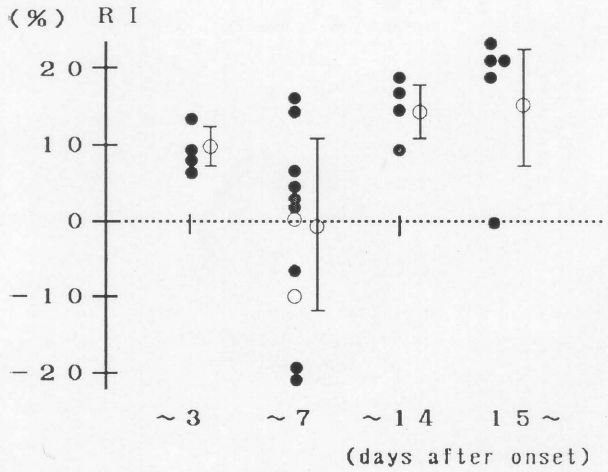

Fig. 2 RIs according to duration after the onset in 23 cases with grade 3. The values have a tendency to increase with time after the onset. From 4 to 7 days, the values varied from −20.1 to +16.0. Two open circles show results for 2 ROIs on the same SPECT image which had different redistribution patterns.

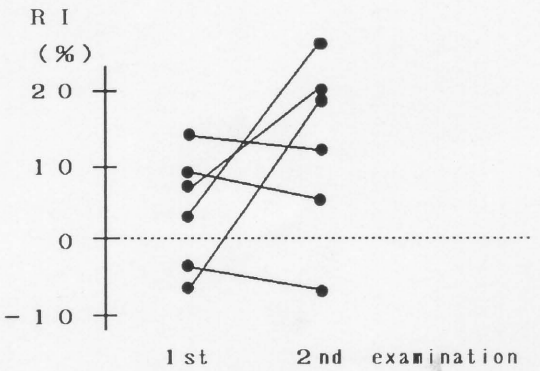

Fig. 3 Changes in RI in 6 cases in grade 3 group. The values were higher in 3 cases and lower in 3 cases at the time of second examination. There is little relationship between RIs at the first examination and those at the second examination.

(lower than zero) in 4 cases, which means 'reversed' redistribution.

In grade 3 group, follow up examinations were performed in 6 cases. The RI in each case is shown in Figure 3. The values were higher in 3 cases and lower in 3 cases in the second examination. In one of 2 cases with a minus RI value in the first examination, it became very high in the second examination. However, the RI became lower in the second examination in the another case.

Case 1.

A fifty-four-year-old man with left hemiplegia. Acute cerebral infarction (Embolism of right middle cerebral artery) in a grade 3 patient. CT was performed on the second day after the onset and showed a low density area (3×5 cm) in the left frontal lobe and the basal ganglia. Figure 4a shows an early IMP image 4 days after the onset. A low perfusion area was observed in the left frontal and temporal lobe. A delayed image in the same patient shows a little redistribution (Fig. 4b). RI was −5.8. An early image in the same patient as in Fig. 4. at 26 days after the onset shows a low perfusion area larger than in Figure 4 (Fig. 5a). Figure 5b shows a delayed image. Good redistribution was observed and the RI was 16.3. Improvement in clinical symptom was also observed in this case.

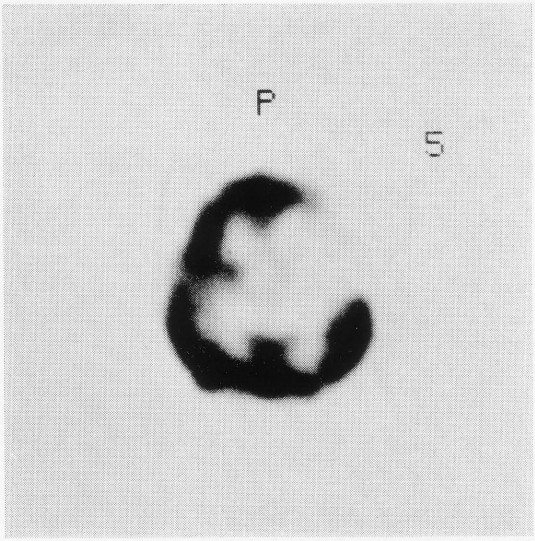

Fig. 4a Early IMP image in grade 3 patient with left hemiplegia at 4 days after the onset. A low perfusion area was observed in the left frontal and temporal lobe.

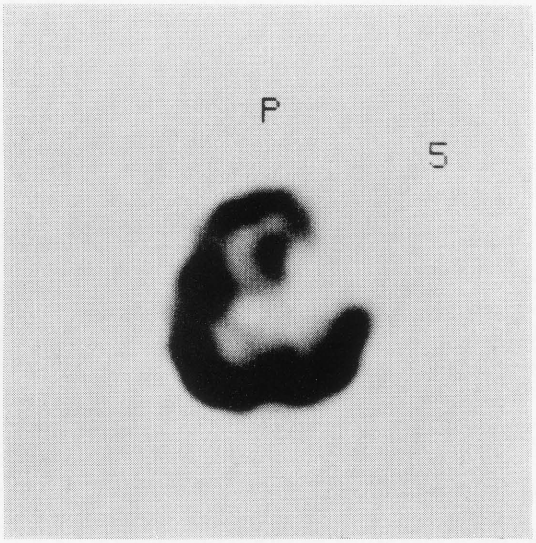

Fig. 4b Delayed image in the same patient showed no redistribution. RI was −5.8.

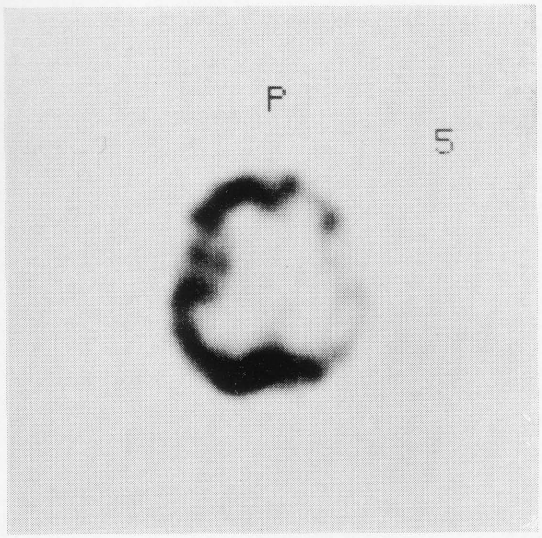

Fig. 5a Early image in the same patient as in Fig. 4 26 days after the onset showed a low perfusion area larger than in Fig. 4.

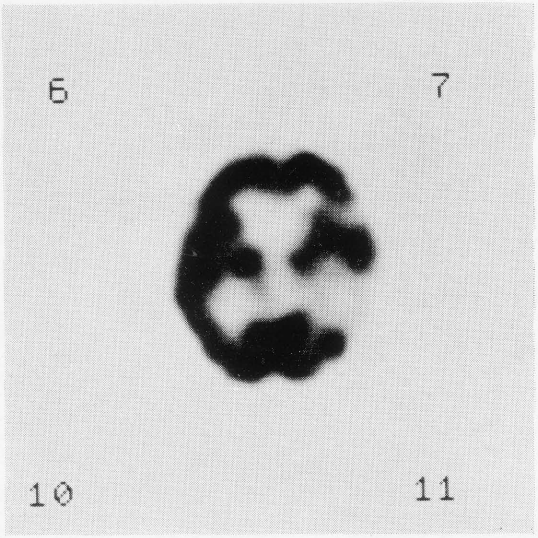

Fig. 6a Early image in patient with right hemiplegia and homonymous hemianopsia at 8 days after the onset. A low perfusion area was observed in the left temporal lobe.

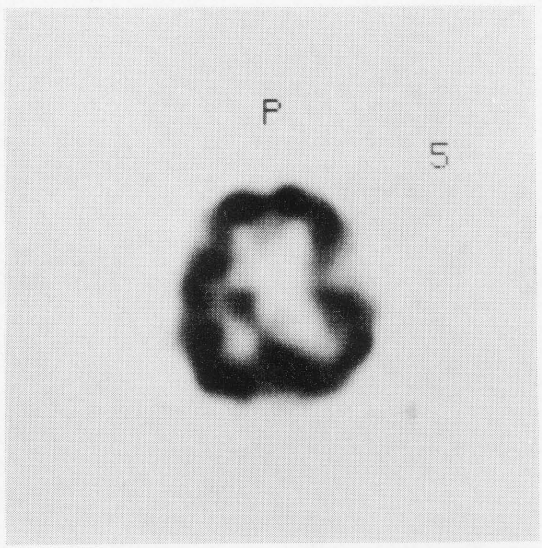

Fig. 5b Delayed image showed good redistribution RI was 16.3. Clinical improvement was also observed.

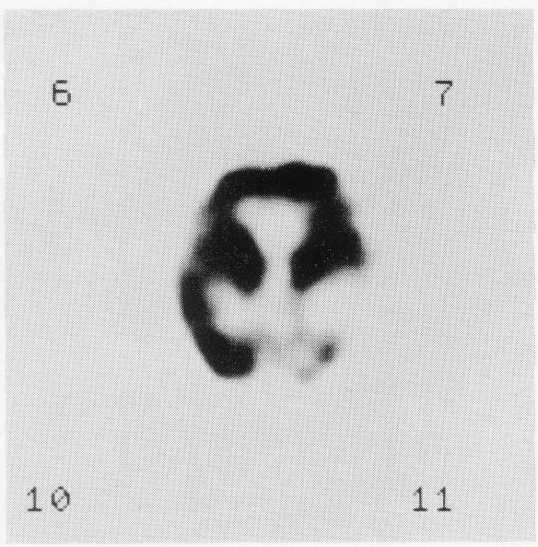

Fig. 6b Delayed image in the same patient. Note low perfusion area in the left occipital lobe as well as in the left temporal lobe.

Case 2.

Eighty-four-year-old woman with right hemiplegia and homonymous hemianopsia. Acute cerebral infarction (Thrombosis of left internal carotid artery) in a grade 3 patient. CT was performed on the second day after the onset and showed a low density area (3×4 cm) in the left temporal and occipital region. Figure 6a shows an early image 7 days after the onset. A low perfusion area was observed in the left temporal lobe. Figure 6b shows a delayed image in the same patient. 'Reversed' redistribution was observed in the left occipital lobe.

DISCUSSION

IMP is clinically used for various cerebral diseases.[1,2] The initial uptake of IMP in the normal brain is proportional to regional cerebral blood flow. IMP SPECT images at an early stage after intravenous injection of IMP is also proportional to regional cerebral blood flow detected by the Xe-133 inhalation method in cerebrovascular disease.[5] Creutzig H et al. reported that depression of activity ranged from 38 to 80% of that on the opposite side in patients with middle cerebral occlusion at 2–4 weeks after stroke.[6] On the other hand, Moretti et al. reported

that the IMP SPECT may not reflect regional cerebral blood flow accurately in cases with luxury perfusion syndrome during the subacute phase of cerebral infarction in contrast to ^{99m}Tc-HMPAO which is also widely used as an rCBF imaging agent.[7] They reported a discrepancy between IMP and ^{99m}Tc-HMPAO uptake in cases with subacute cerebral infarction and explained that this phenomenon is caused by a reduction in the extraction fraction of IMP due to tissue acidosis. In this phase of stroke, however, the ^{99m}Tc-HMPAO SPECT image resembles the rCBF image and the IMP SPECT image resembles those of the regional $CMRO_2$ ($rCMRO_2$) obtained by positron emission tomography.[7] $rCMRO_2$ is one of informations on the cerebral metabolism which is not proportional to rCBF in abnormal brain tissue.

Furthermore, the distribution of IMP changes with time. Redistribution or 'filling in' phenomena were observed in white matter in the normal brain.[8] In the delayed IMP SPECT images, redistribution or 'filling in' phenomena were also observed in the ischemic area, which may be useful in establishing the prognosis and evaluating the efficacy of therapy in stroke cases.[3,4] Tsukuda et al reported that good redistribution was observed in the lesions with moderately high rCBF and $rCMRO_2$ in ischemia or subacute phase of infarction, but poor redistribution was observed in those with low rCBF and $rCMRO_2$ in chronic infarction.[9]

In our study, good redistribution was obtained in the grade 1 and grade 2 groups. In the grade 3 group, poor redistribution was observed and the RIs ranged from −20.1 to 22.8. The standard deviations of L/T ratios in this group were also large in both early and delayed images. These findings show that good redistribution was observed in normal density areas in the CT image, on the other hand, the degree of redistribution differs very much in low density areas in the CT image.

The redistribution index is low and standard deviation is the greatest between 4 days and 7 days after the onset in the acute stage. Minus RI means 'reversed' redistribution which was observed in 4 patients. Minus RIs were not observed earlier than 3 days or later than 8 days after the onset. This is a characteristic phenomenon at this stage after the onset. This 'reversed' redistribution is observed in the damaged brain tissue, which makes it difficult to interpret the delayed IMP SPECT image. The mechanisms of IMP uptake and retention in the brain are considered that IMP binds to the nonspecific receptors and IMP is metabolized into impermeable metabolites which do not cross blood brain barrier.[2,10,11] In low density areas in the acute stage, function of brain tissue is affected although neurons and synaptosomes may not be damaged. The ischemic brain tissue uptakes IMP by binding to the receptor. The damaged brain tissue may not metabolize IMP, and IMP may be washed out from the tissue in the early phase.

Follow up examinations were performed in 6 patients in the grade 3 group. The values became higher in the second examination in 3 cases and lower in 3 cases. In one of 3 cases with minus RI, RI became very high in the second examination and the clinical symptom (hemiplegia) also improved. However, RI became lower in the second examination in another case. As the relationship between the change in RI in the first examination and the second examination was not clear, the threshold level of L/T ratio or RI of good prognosis could not be found out. Further investigation is needed to evaluate the redistribution phenomenon in the delayed image in acute CVD.

In conclusion, good redistributions were observed in grade 1 and 2 groups, and the prognoses were good. On the other hand, poor redistributions were observed in the grade 3 group. There was not a close relationship in the degrees of redistributions or 'reversed' redistribution between the first and second examinations in the grade 3 group.

REFERENCES

1. Kuhl DE, Barrio JR, Huang SC, et al: Quantifying local cerebral blood flow by N-isopropyl-p-[^{123}I] iodoamphetamine (IMP) tomography. *J Nucl Med* 23: 196–203, 1982
2. Holman BL, Hill TC, Lee RGL, et al: Brain imaging with radiolabeled amines. *In Nuclear Medicine Annual* 1983. Freeman LM, Weissman HS, eds. New York, Raven Press: 131–165, 1983
3. Raynaud C, Rancurel G, Samson Y, et al: Pathophysiologic study of chronic infarcts with I-123 isopropyl iodo-amphetamine (IMP): The importance of peri-infarct area. *Stroke* 18: 21–29, 1987
4. Defer G, Moretti JL, Cesaro P, et al: Early and delayed SPECT using N-isopropyl p-iodoamphetamine iodine 123 in cerebral ischemia. A prognostic index for clinical recovery. *Arch Neurol* 44: 715–718, 1987
5. Lassen NA, Henrikson L, Holm S, et al: Cerebral bloodflow tomography Xenon-133 compared with isopropyl-amphetamine-iodine-123: Concise communication. *J Nucl Med* 24: 17–21, 1983
6. Creutzig H, Schober O, Gielow R, et al: Cerebral Dynamics of N-isopropyl-(^{123}I) p-iodoamphetamine. *J Nucl Med* 27: 178–183, 1986
7. Moretti JL, Defer G, Cinotti L, et al: "Luxury perfusion" with ^{99m}Tc-HM-PAO and ^{123}I-IMP SPECT imagings during the subacute phase of stroke. *Eur J Nucl Med* 16: 17–22, 1990
8. Hoshi H, Jinnouchi S, Watanabe K, et al: Biodistribution of N-isopropyl-p-iodoamphetamine in the Rat

Brain. *Nuclearmedizin* 26: 131–134, 1987
9. Tsukuda M, Kuwabara Y, Ichiya Y, et al: Evaluation of the significance of "redistribution" in I-123 IMP SPECT in cerebrovascular disorders—a comparative study with PET. *Eur J Nucl Med* 15: 746–749, 1989
10. Winchell HS, Baldwin RM, Lin TH: Development of I-123-labeled amines for brain studies: Localization of I-123 iodophenylalkyl amines in rat brain. *J Nucl Med* 21: 940–946, 1980
11. Winchell HS, Horst WD, Braun L, et al: N-isopropyl-^{123}I p-iodoamphetamine: single-pass brain uptake and washout; binding to brain synaptosomes; and localization in dog and monkey brain. *J Nucl Med* 21: 947–952, 1980