

Assessment of Demented Patients by Dynamic SPECT of Inhaled Xenon-133

Akio Komatani, Koichi Yamaguchi, Yukio Sugai,
Toshiyasu Takanashi, Masahiro Kera,
Masao Shinohara, and Shinobu Kawakatsu

*Department of Radiology and Neuropsychiatry, Yamagata University School of Medicine,
Zao-Iida Yamagata, Japan*

We studied the potential for using dynamic single photon emission computed tomography of inhaled xenon-133 (¹³³Xe) gas in the assessment of demented patients. An advanced ring-type single photon emission computed tomography (SPECT) "HEADTOME" with improved spatial resolution [15 mm in full width at half maximum (FWHM)] was used for tomographic measurement of regional cerebral blood flow (rCBF). All 34 patients underwent a detailed psychiatric examination and x-ray computed tomography scan, and matched research criteria for Alzheimer's disease (n = 13), senile dementia of the Alzheimer type (n = 9), or multi-infarct dementia (n = 12). In comparison with a senile control group (n = 7), mean CBF of both the whole brain and the temporo-parietal region was significantly less in the Alzheimer's disease and senile dementia Alzheimer type groups, but no significant difference was seen between the senile control group and multi-infarct dementia group. The correlation was 0.72 (p < 0.004) between the mean CBF of the whole brain and the score of Hasegawa's Dementia Scale, and 0.94 (p < 0.0001) between rCBF of the temporo-parietal region and the scale in Alzheimer's disease. In the senile dementia Alzheimer type group, the correlations were 0.77 (p < 0.01) and 0.83 (p < 0.004) respectively. No significant correlations were found in the multi-infarct dementia group. A temporo-parietal reduction in the distribution of the rCBF characteristic in the Alzheimer's disease group and a patchy whole brain reduction characteristic in the multi-infarct dementia group was detected. The ability of our improved SPECT to provide both quantitative measurement of rCBF and characteristic rCBF distribution patterns, makes it a promising tool for research or routine examination of demented patients.

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The xenon-133 (¹³³Xe) gas inhalation technique for the measurement of regional cerebral blood flow (rCBF) is a very practical method for routine examination because of its simplicity and its ready availability for emergency. We previously reported the technical points for improvement of spatial resolution and quantitative measurement of our "HEADTOME" system (1,2). Based on this improvement, the potential applications of ¹³³Xe inhalation single photon emission computed tomography (SPECT) in the examination of demented patients have been studied.

MATERIALS AND METHODS

Patients

All patients were in the early or early middle stage of dementia. They underwent a detailed neuropsychological examination [DSM-3 (3), Hachinski's score (4)], laboratory tests and x-ray computed tomography (CT) scan, and matched research criteria for either Alzheimer's disease, senile dementia of Alzheimer type, or multi-infarct dementia. Thirteen pa-

TABLE 1
Subject

		Age (yr)
Senile control	(n = 7)	66-77
Alzheimer's disease	(n = 13)	36-72
Senile dementia of the Alzheimer type	(n = 9)	70-79
Multi-infarct dementia	(n = 12)	57-75

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For reprints contact: A. Komatani, Dept. of Radiology and Neuropsychiatry, Yamagata University School of Medicine, Zuo-Iida Yamagata, 990-23 Japan.

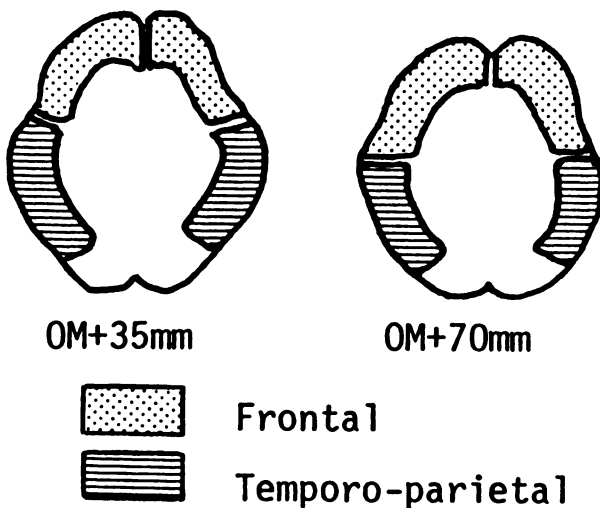


FIGURE 1
Scheme of ROI. The mean values of the corresponding ROI on the two planes (OM+35, 70 mm) were used for the quantitative analysis.

tients with Alzheimer's disease (from 36 to 72 yr, mean = 58 yr), nine patients with senile dementia Alzheimer type (70-79 yr, mean 73 yr) and 12 patients with multi-infarct dementia (57-75 yr, mean 69 yr) were compared with a senile control group (69-77 yr, mean 71 yr, n = 7). The senile control group consisted of some members in a circle of gate-ball that is one of the most popular sports for senile people in Japan. They were active in good health and their mean CBF was little inferior to that of middle aged normal group (29-56 yr, mean = 47 yr, n = 27) with mean CBF of 51.5 ± 4.5 ml/100 g/min. Only the senile control group was used as a comparative control in this study. The subjects are summarized in Table 1.

TABLE 2
Eleven Questions with Weighted Scores from Hasegawa's Dementia Scale

Questions	Score
1. What is the date today?	0, 3
2. Where are you? (Name of the place?)	0, 2.5
3. What is your age?	0, 2
4. How long have you been here?	0, 2.5
5. Where is your birthplace?	0, 2
6. When did World War II end?	0, 3.5
7. How many days are there in a year?	0, 2.5
8. Who is the Prime Minister?	0, 3
9. Subtract 7 from 100, then 7 from 93.	0, 2, 4
10. Name these numbers in reverse order: 6-8-2, 3-5-2-9.	0, 2, 4
11. Recall the five objects that were presented to you earlier.	0, 0.5, 1.5, 2.5, 3.5
(Full score: 32.5)	

rCBF Measurement

Regional cerebral blood flow (rCBF) was measured tomographically in two planes situated 3.5 cm and 7.0 cm above the orbito-meatal plane, by using a ring-type dynamic SPECT (HEADTOME:SET-021, Shimadzu, Japan) (5,6). Xenon-133 gas was administered by rebreathing through a mouthpiece for 1 min. During this period and the following 5 min of ^{133}Xe washout, a series of six consecutive ^{133}Xe distribution maps of the brain was taken each of 1 min duration. Approximately 50 mCi (1.85 GBq) of ^{133}Xe gas was admixed with atmospheric air in a 2-l spiropag. This results in a maximum counting rate of ~100k counts during the second 1-min period on each plane. Tomographic images were constructed using the filtered backprojection method (Butterworth filter; fm = 15, Order = 8) (7). Cerebral blood flow was calculated by the "sequential picture method" proposed by Kanno and Lassen (8). The spatial resolution in FWHM of our HEADTOME system is

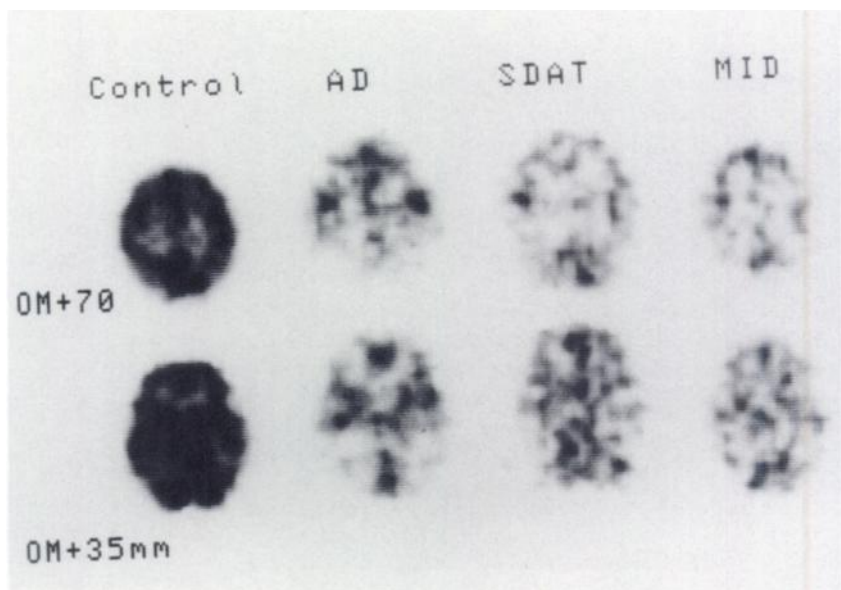


FIGURE 2
Typical patterns of a rCBF image in control, Alzheimer's disease (AD), senile dementia Alzheimer type (SDAT) and multi-infarct dementia (MID) patients.

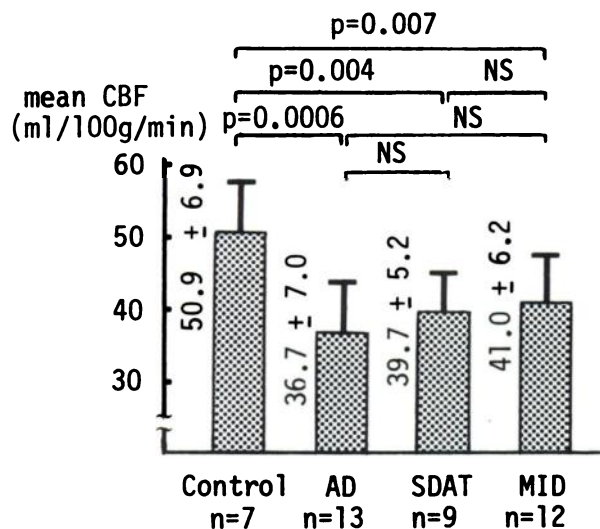


FIGURE 3
Mean CBF, standard deviation (s.d.) and significance levels in tests for differences between the control and demented groups (AD, SDAT, and MID).

~15 mm transversely and 25 mm axially at the center of a cylindrical phantom (20 cm in diameter). The energy window level was adjusted to 75–110 keV (–7.5%~+36%) for the photopeak of ^{133}Xe (81 keV) (9).

Data Analysis

For the quantitative analysis, the regions of interest (ROIs) at the frontal and temporo-parietal cortex derived from x-ray CT and anatomic cross sections were superimposed on each image (Fig. 1). Then the rCBF values were generated, and the mean values of the corresponding ROI on the two planes (OM+35 and OM+70 mm) were used. The mean value of all the region on the two planes was used as a mean CBF of the whole brain.

Classification of the Degree of Dementia

For classification of the degree of dementia, we used the score of Hasegawa's Dementia Scale (10) that has 11 questions with weighted scores (Table 2). This was administered verbally. The maximum score is 32.5 and the degree of dementia is assessed by the total score.

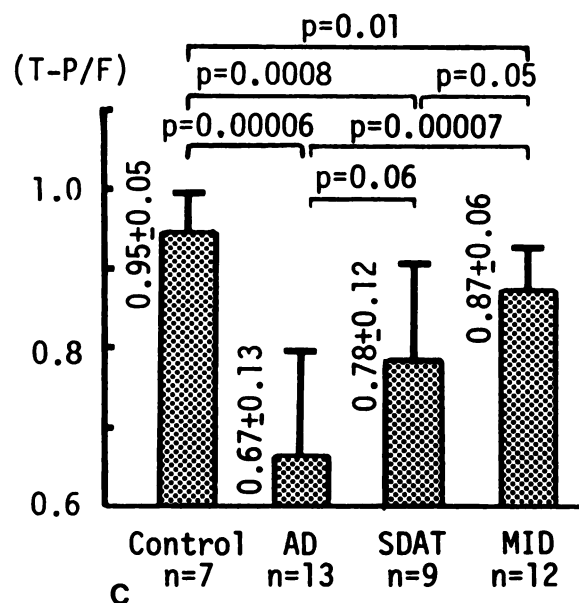
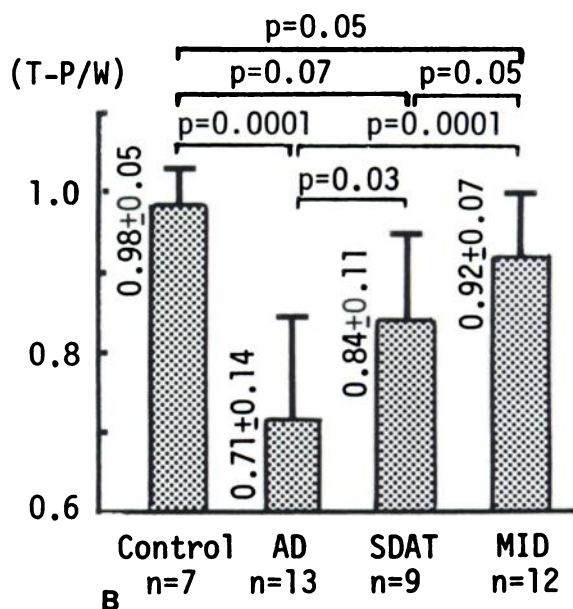
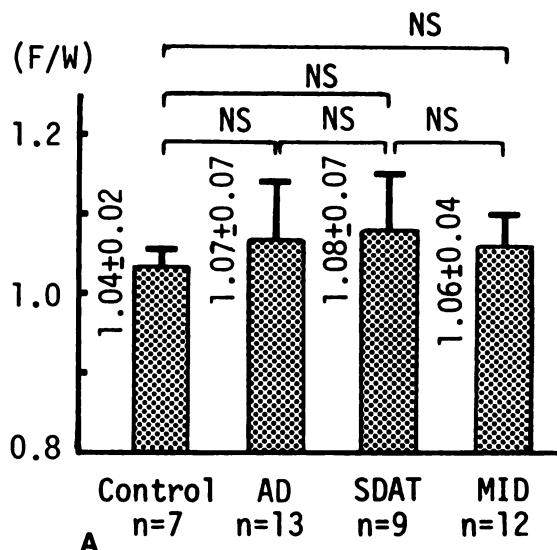
RESULTS

Patterns of rCBF Distribution

Examples of typical patterns of rCBF in senile control and demented patients are shown in Figure 2. There

FIGURE 4

The rCBF ratios of (A) frontal to whole brain (F/W), (B) temporo-parietal to whole brain (T-P/W), and (C) temporo-parietal to frontal (T-P/F). No significant differences are apparent in F/W. The ratio of T-P/W and T-P/F decrease in the order control, multi-infarct dementia (MID), senile dementia Alzheimer type (SDAT), and Alzheimer's disease (AD) and all comparisons among the four groups are significant.



seems to be a CBF reduction in the demented patients compared with the senile control. In particular, symmetrical temporo-parietal reduction was remarkable in Alzheimer's disease and senile dementia Alzheimer type. A patchy reduced pattern was commonly seen in the multi-infarct dementia patients. For the quantitative analysis of demented patients, the mean CBF in the whole brain were compared among the groups. The mean CBF, standard deviation (s.d.) and significance-levels obtained by t-test for differences between the senile control and the three demented groups are illustrated in Figure 3. The mean CBF value in the demented groups were significantly lower than those in the senile control group, but no significant difference was seen among the three demented groups.

To characterize the pattern of rCBF distribution, we calculated the rCBF ratio of the frontal region to the whole brain (F/W), the temporo-parietal region to the whole brain (T-P/W) and the temporo-parietal to the frontal region (T-P/F), and compared these ratios across groups. The ratio of F/W ranged from ~1.0 to 1.1 in all groups and no significant difference were apparent (Fig. 4A). On the other hand, the ratios of both T-P/W and T-P/F showed the same sequential decrease in the order senile control, multi-infarct dementia, senile dementia Alzheimer type, and Alzheimer's disease and all comparisons among the four groups were significant (Fig. 4B,C).

Correlation Between rCBF and Degree of Dementia

Cerebral blood flow was found to be in proportion to the score on the Hasegawa's Dementia Scale in the Alzheimer's disease group. The rCBF image in four

cases with scales of 27.0, 17.0, 12.0 and 0 are shown (Fig. 5). Cerebral blood flow in the whole brain, the frontal region, and the temporo-parietal region was compared with the scale in the various types of dementia. In the Alzheimer's disease group, cerebral blood flow showed the highest correlation with the scale, especially in the temporo-parietal region with a correlation coefficient of 0.94 ($p < 0.0001$) (Fig. 6A). Also in the senile dementia Alzheimer type group, rCBF of the temporo-parietal region correlated more highly with the Hasegawa's Dementia Scale than the frontal region or the whole brain did, but this correlation was not as high as that seen in the Alzheimer's disease group (Fig. 6B). In the case of multi-infarct dementia, no significant correlation between cerebral blood flow and scale was seen at all (Fig. 6C).

DISCUSSION

The previous investigation of rCBF changes in dementia using ^{133}Xe and external counting techniques produced varying results (11-15). Our SPECT studies have shown a high incidence of temporo-parietal reduction in Alzheimer's disease and senile dementia Alzheimer type, as has previously been reported using positron emission computed tomography (PET) (16-26). Also a patchy reduced pattern is commonly seen in multi-infarct dementia patients. However, the quantitative analysis of early and early middle staged dementia by the ^{133}Xe inhalation SPECT has not been reported.

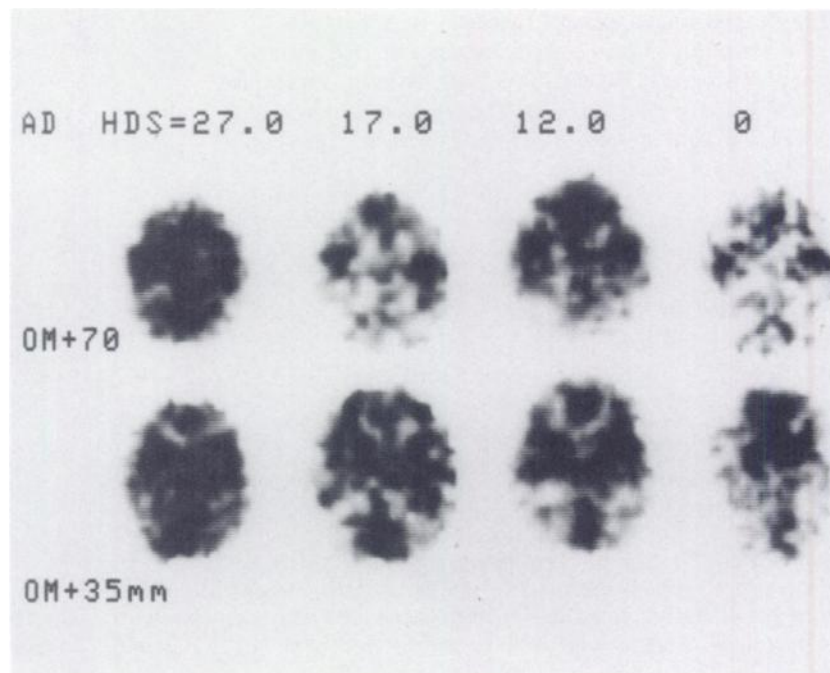


FIGURE 5
rCBF images of Alzheimer's disease (AD) at various stages according to the score of Hasegawa's Dementia Scale (HDS).

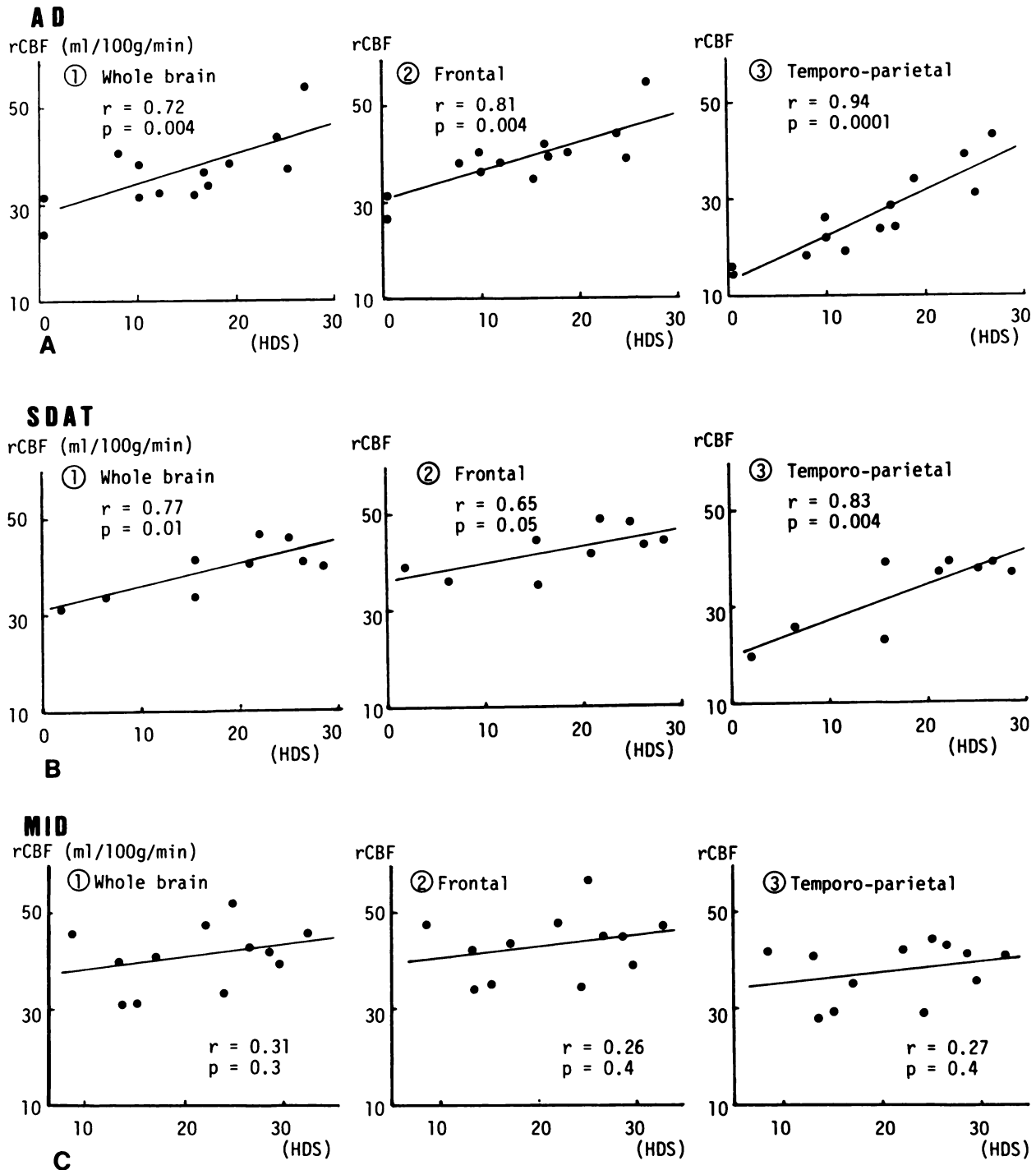


FIGURE 6

Cerebral blood flow of the whole brain, frontal region and temporo-parietal region vs. the score of Hasegawa's Dementia Scale (HDS) for (A) Alzheimer's disease (AD), (B) senile dementia Alzheimer type (SDAT), and (C) multi-infarct dementia (MID).

The rCBF ratios of the temporo-parietal region to the whole brain and the temporo-parietal to the frontal region do serve to characterize each group. It seems to be possible to distinguish between the senile control, and demented groups using these ratios. However, using the mean CBF of the whole brain, it is possible to

distinguish between the senile control and demented groups, but not the demented groups from one another.

Cerebral blood flow was reduced in proportion to the severity of dementia in Alzheimer's disease and senile dementia Alzheimer type, especially in the temporo-parietal region, but no significant correlation between

CBF and the Hasegawa's Dementia Scale was seen in the multi-infarct dementia group. So it may be possible to estimate the degree of dementia objectively in the cases of Alzheimer's disease and senile dementia Alzheimer type.

CONCLUSION

The ability of our ^{133}Xe inhalation SPECT to provide quantitative measurement of rCBF and to detect characteristic rCBF distribution patterns makes it a promising tool for research or for routine examination of demented patients.

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