

Three-Dimensional Display of Surface Cortical Perfusion by SPECT: Application in Assessing Alzheimer's Disease

Kazuo Hashikawa, Masayasu Matsumoto, Hiroshi Moriwaki, Naohiko Oku, Yutaka Okazaki, Yujiro Seike, Toshiisa Uehara, Hirotaka Tanabe, Yasuhide Ohie, Takenobu Kamada and Tsunehiko Nishimura

Department of Nuclear Medicine, First Department of Internal Medicine, Third Division Medical Science for Health, Faculty of Health and Sports Science, and Division of Tracer Kinetics, Biomedical Research Center, Osaka University Medical School, Suita, Japan; and Hitachi Medical Corporation, Chiba, Japan

To better understand cortical perfusion, we developed a method for a three-dimensional display technique with ^{99m}Tc -hexamethylpropyleneamine oxime (HMPAO) SPECT. **Methods:** Twelve patients with higher cortical dysfunction due to Alzheimer's disease and 18 age-matched controls were examined. Data acquisition was performed after intravenous injection of 740 MBq of ^{99m}Tc -HMPAO. After reconstructing the transaxial images, the three-dimensional images were obtained by modified volume rendering, where the surfaces were displayed in the corresponding colors as the maximum cortical value within a depth of 2 cm. **Results:** In the control studies, almost all surface cortices were over 60% of the maximum cerebellar value. In Alzheimer's disease patients, areas of perfusion below 60% were detected in the temporo-parietal lesions and frontal lobe lesions in 6 of 12. These findings correlated with the neurological dysfunction. **Conclusion:** This method provides realistic three-dimensional information about surface cortical perfusion, which was found to be useful in clinical investigations of higher cortical dysfunction due to degenerative or cerebrovascular diseases.

Key Words: three-dimensional display; single-photon emission computed tomography; Alzheimer's disease; cognitive dysfunction

J Nucl Med 1995; 36:690-696

The evaluation of surface perfusion is important when investigating higher cortical neuronal function under physiological and pathological conditions. To display regional cerebral blood flow (rCBF) obtained by emission computed tomography, three sets of tomographic images (transaxial, coronal, sagittal) are generally used. Although the rCBF values of the whole brain from the surface to deep structures are included in these conventional displays, many slices must be carefully examined to comprehend the

three-dimensional extent of a lesion. We therefore developed a means to display surface cortical perfusion from SPECT data that offers a realistic three-dimensional image of surface cortical perfusion.

MATERIALS AND METHODS

Patient Selection

We studied 12 patients with Alzheimer's disease (Group A; age = 57.7 ± 10.1 yr (mean \pm s.d.); 8 males and 4 females) who had more than two neurological deficits, including amnesia. Probable Alzheimer's was diagnosed in accordance to NINCDS-ADRDS criteria (1). MRI revealed no ischemic lesions and no episode-like cerebrovascular diseases. For the control group, 18 age-matched patients (Group C; age = 58.7 ± 9.7 ; 15 males and 3 females) were studied. They suffered headaches or dizziness, and had no abnormalities according to computed tomography (CT), MRI and neuropsychological examinations. Cognitive deficits were investigated by a neuropsychologist (H.T.), and dementia severity was evaluated by the Mini-Mental State Examination (MMSE) and Raven's Colored Progressive Matrices (RCPM).

Scanning Procedures

All SPECT studies were performed with a four-head rotating SPECT system (2). The spatial resolution was 9.8 mm FWHM for both transaxial and longitudinal directions; low-energy, high-resolution collimators were used. Data acquisition started 5 min after intravenous injection of 740 MBq ^{99m}Tc -HMPAO. The number of angular samplings was 64 or 128. The acquisition time per step was 15-30 sec and the acquisition matrix was 64×64 (1 pixel = 4×4 mm). These protocols are used for routine studies in our institute and no special acquisition was made for this three-dimensional display of cortical perfusion (3D-CBF image).

Data Processing

Data were processed with a Hitachi Advanced Radionuclide Processor II, which has a 16-bit minicomputer central processing unit equipped with a 256 kW (512 kB) memory. Image reconstruction was performed with a Butterworth prefilter and a Ramachandran filter. Attenuation correction was made with a postreconstruction method (3). Diameters of the oval shape for attenuation correction were determined for each slice from the anterior and left lateral views of the original projection images. After reconstruction, 42 slices at 4 mm pitch transaxial images were obtained.

Received Apr. 11, 1994; revision accepted Sept. 30, 1994

For correspondence or reprints contact: Kazuo Hashikawa, MD, First Department of Internal Medicine, Osaka University Medical School, Yamadaoka 2-2, Suita 565, Japan.

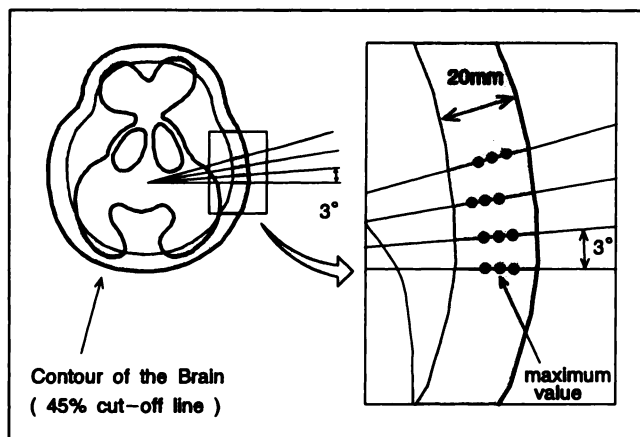


FIGURE 1. A schematic display of three-dimensional surface cortical flow. The mean of the maximum value and two neighboring values in one radius was substituted in the corresponding surface (the point of intersection between the radius and the contour of the brain).

Due to the computer's capacity, 32 slices were then selected for processing as follows. These 32 consecutive transaxial images at 4 mm pitch covered 128 mm longitudinally and were sufficient for whole-brain imaging, including the cerebellum. The 32 selected images in the 64×64 matrix were converted into 63 transaxial images in a 128×128 matrix by interpolation. Thereafter, the contour of the brain in each slice was determined by the 45% iso-accumulation line of the maximum value of the whole brain. If the contour of the brain could not be detected due to a perfusion defect or a low perfusion area, the line obtained from the 45% iso-accumulation was manually modified and contrasted with CT or MR images. The transaxial images were translated to two-dimensional polar co-ordinates at three-degree steps. The maximum value in one direction between 2 cm thickness from the surface was identified. Following surface identification, mean of the three values, maximum and the two values in front and behind the maximum in the radius were substituted into the corresponding surface as the cortical value (Fig. 1). The three-dimensional images were shown by volume-rendering in a 14" color display with a color scale in proportion to surface values. A rainbow color

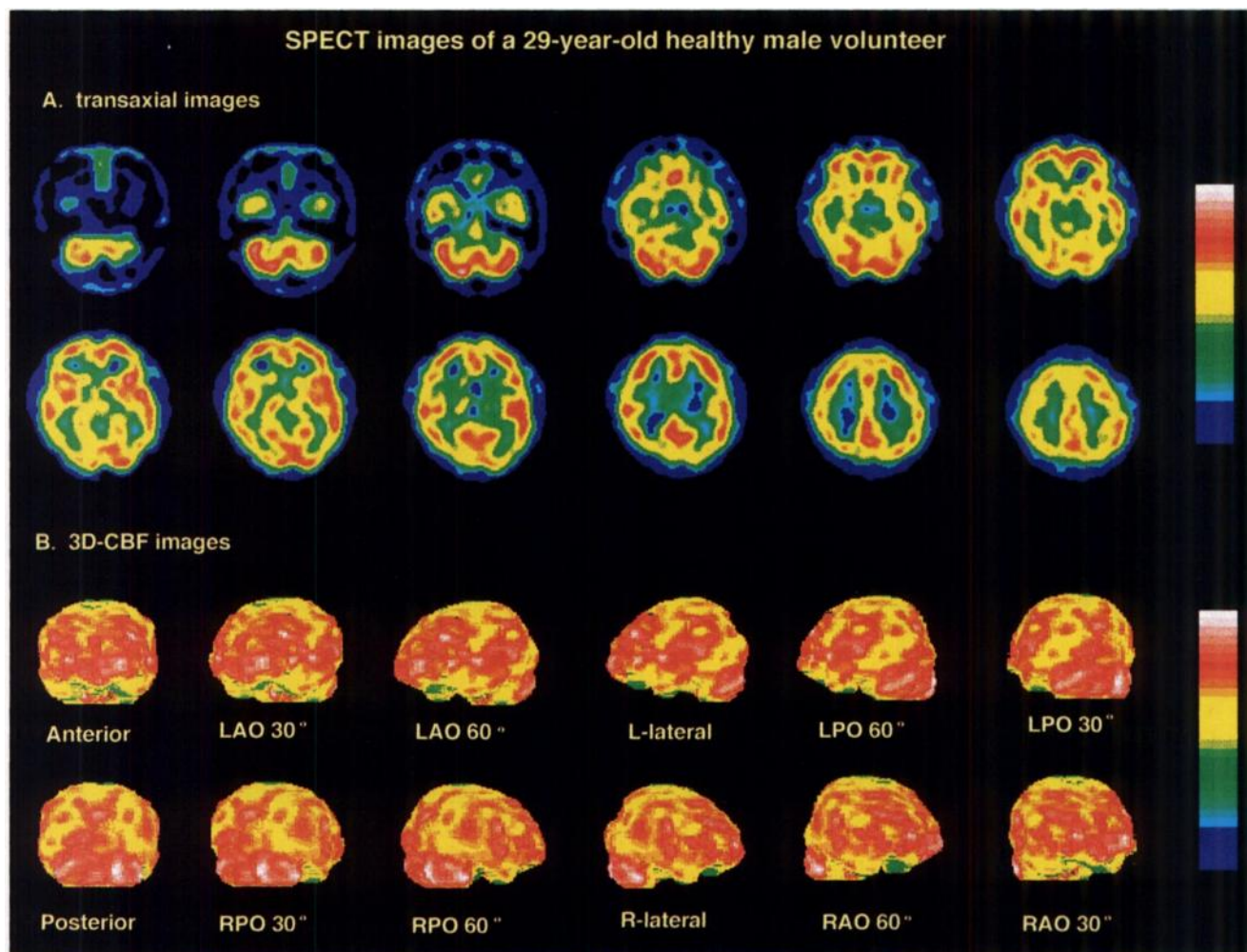


FIGURE 2. SPECT transaxial (A) and three-dimensional CBF images (B) of a 29-yr-old healthy male volunteer. (b) Three-dimensional perfusion images were viewed from 12 directions with rotation at 30-degree steps from anterior view. Almost all of the surface is in red and yellow, which corresponds to homogeneous rCBF around the surface cortex.

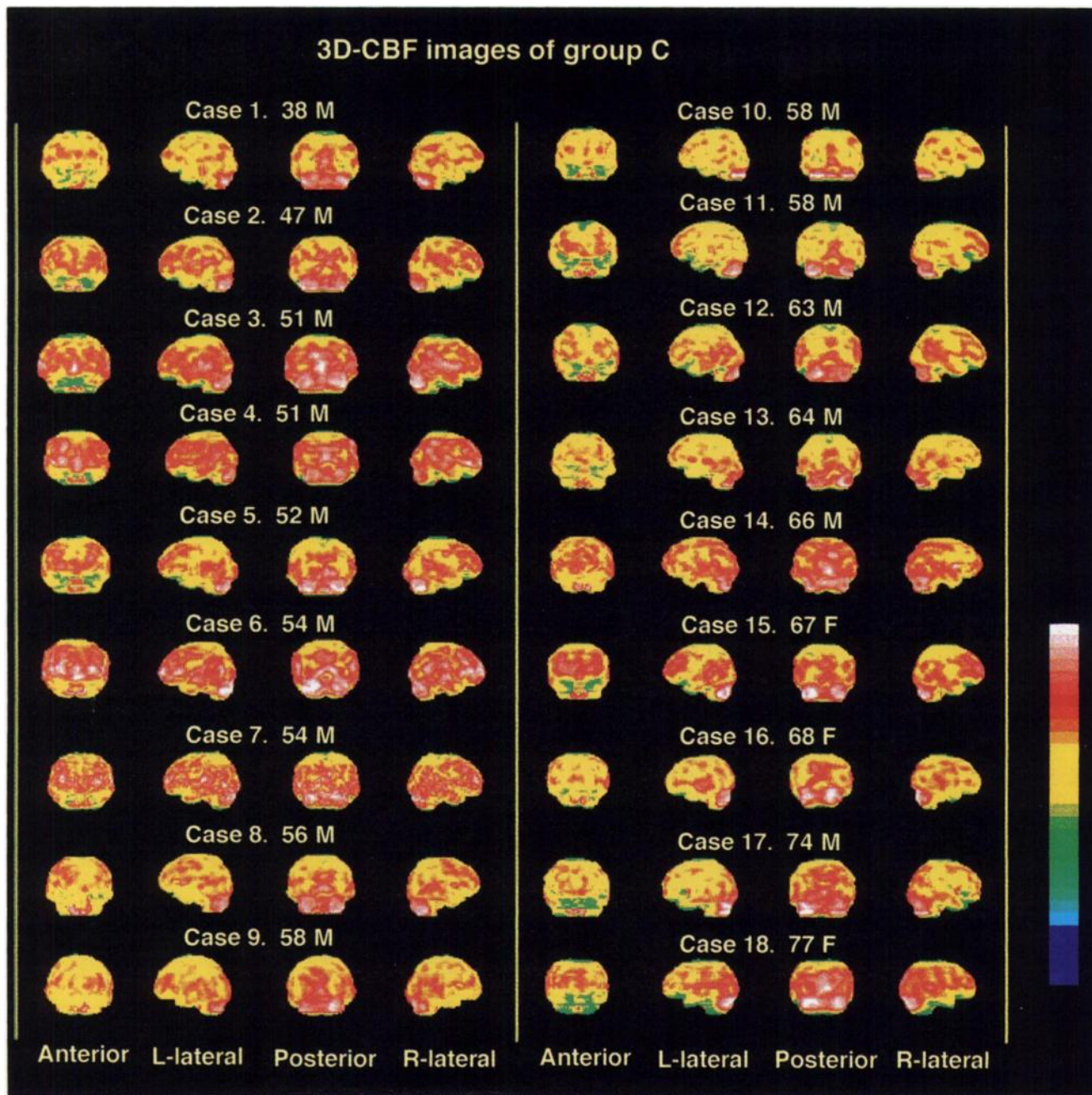


FIGURE 3. The three-dimensional CBF images of the patients in Group C. Almost all cortices were displayed in red or yellow; meaning perfusion of the surface cortices was more than 60% of the maximum of the cerebellum. There were slightly low perfusion, spotty lesions in the temporo-occipital lesions, which were colored yellowish green, ranging from 57% to 60% of the maximum of the cerebellum. These lesions were easily distinguishable from temporoparietal lesions of Alzheimer's disease in Figure 4.

scale was used in which the maximum value of the cerebellum was displayed in white; the remaining lesions were shown in whitish pink, pink, red, yellow, yellowish green, green, sky blue, dark blue and black, according to the rCBF in descending order. Each color thus corresponded to the percent accumulation of the maximum of the cerebellar hemisphere. The images could be freely rotated upon two axes, therefore providing a realistic perfusion image from any direction. All processing required about 40 min to complete, including translating the original SPECT data into the three-dimensional CBF image.

RESULTS

Figure 2 shows transaxial images and three-dimensional CBF images of a 29-yr-old healthy male volunteer. The three-dimensional CBF images show that no cortical lesions had lower flow than yellow (60% accumulation of the maximum). Figure 3 shows a summary of the three-dimensional CBF images of Group C. The flow was higher than that of yellow in almost all the surface cortices, except for some small spotty lesions. We therefore defined that the

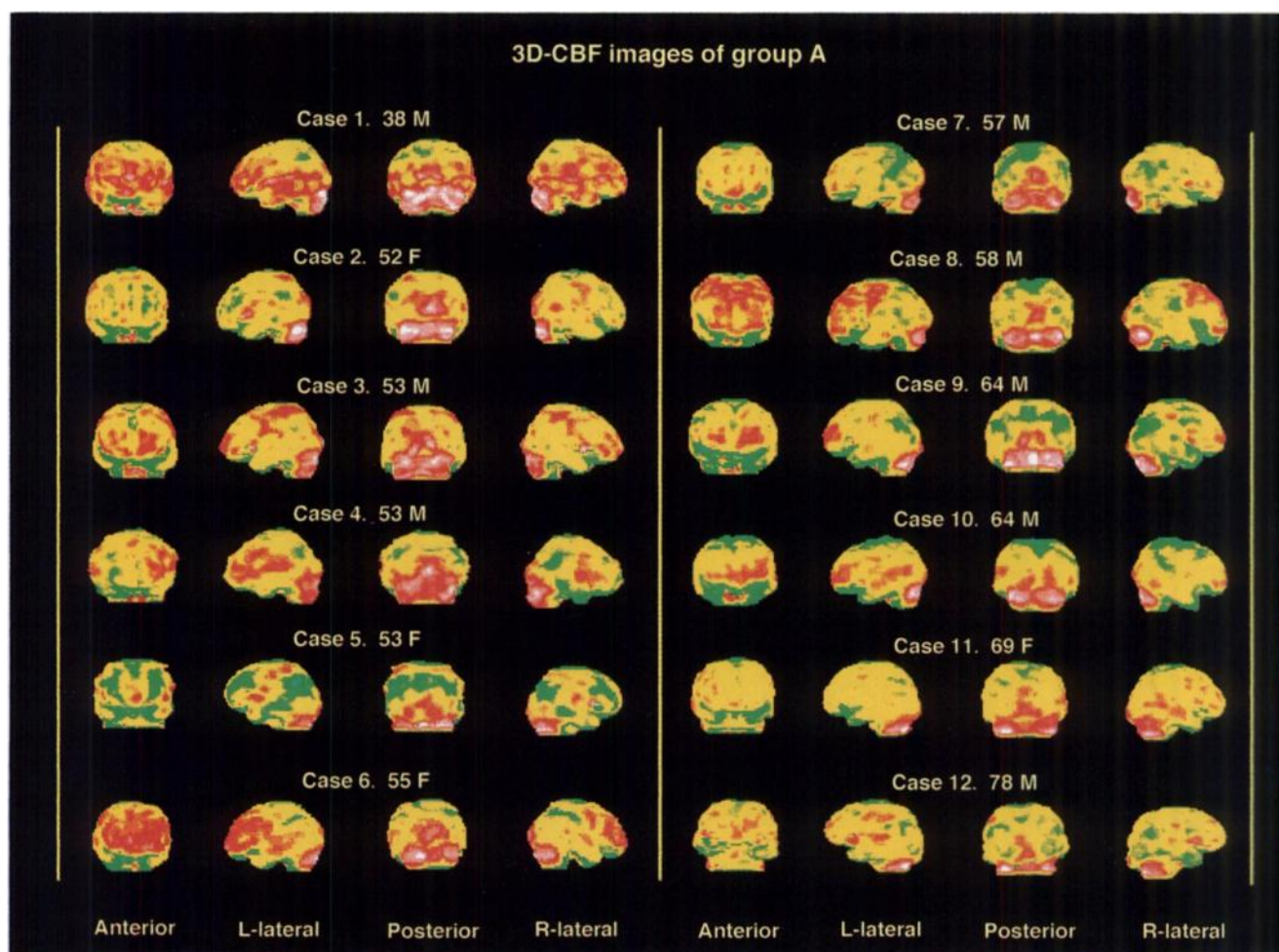


FIGURE 4. The three-dimensional CBF images of cortical perfusion in Group A patients. The regions, which were considered to have abnormal low perfusion, corresponded with the neurological deficits of the patients (Table 1). In Patient 1, the low perfusion area in the left parietal lobe was demonstrated more clearly than in transaxial images (Fig. 5). In Patient 5, we can see the remarkable reduction of rCBF in the most of cortices except the primary sensorimotor areas. In Patient 8, the temporoparietal lesions ranged over almost all parietal and temporal lobes, and the primary sensorimotor cortex was also involved, which was considered to be related to symptoms of clumsiness. In Patient 11, the low perfusion area in the left parietal lobe was obscure in the transaxial images (Fig. 5), however, they were clearly resolved in the three-dimensional CBF images.

lesions displayed in colors below yellow, which is presented as less than 60% of the maximum value of the cerebellum, were abnormal low perfusion areas. Figure 4 shows three-dimensional CBF images of Group A. Temporoparietal (TP) lesions, the characteristic three-dimensional pattern of areas affected by Alzheimer's disease (4), are displayed in the abnormal low perfusion area of all patients. Bilateral TP lesions were evident in nine patients, left TP in two and right TP in one. Severed low perfusion in the right hemisphere was evident in Patient 8, in whom left unilateral spatial neglect was revealed. The frontal lobe was involved in six patients. In three of these patients (Patients 2, 4, 5), who had apparent low perfusion areas in the frontal lobe, the representative symptom of frontal lobe involvement and personality change was seen clinically. These results indicate that the areas displaying less than 60% accumulation of the maximum correlated well with their cognitive deficits (Table 1). Almost all of the low

perfusion areas in the three-dimensional CBF images could also be seen in the transaxial images, but their anatomical relationships were comprehended more easily in the three-dimensional CBF images (Figs. 4, 5).

DISCUSSION

All rCBF data of the whole brain are included in each set of images. To comprehend the nature of cortical perfusion, however, multiple slices must be examined, and experience in interpreting three-dimensional imaging is required. Consequently, we developed a method of three-dimensional CBF display that offers a realistic spatial image of surface cortical perfusion. The method was based on circumferential display combined with a three-dimensional approach. The circumferential analysis is commonly used in thallium myocardial SPECT (5,6) and has been applied to brain SPECT data to quantify cortical blood flow (7-10).

TABLE 1
Patient Summaries (Group A)

Patient no.	age (yr)	sex	Neurological dysfunctions						MMSE (/30)	RCPM (/36)	3D-CBF findings low perfusion areas
			MD	VSD	WFD	AC	LOI	PC			
1	38	M	+	+	±	+	+	—	np	IM	BILTP(L>R)
2	52	F	+	+	+	+	+	+	9	IM	BILF, LTP
3	53	M	+	+	—	+	+	—	11	22	BILTP
4	53	M	+	+	—	+	+	+	np	29	R.F, BILTP(R>L)
5	53	F	+	+	+	+	+	+	np	IM	BILF, BILTP
6	55	F	+	+	—	+	±	—	21	20	BILTP
7	57	M	+	+	—	+	—	—	25	18	BILTP
8	58	M	+	+	+	+	±	—	11	IM	BILTP(R>L)
9	64	M	+	+	+	+	±	—	7	IM	R.F, BILTP(R>L)
10	64	M	+	+	+	+	+	—	14	21	R.F, R.TP
11	69	F	+	—	±	—	—	—	23	35	LTP
12	78	M	+	+	+	+	+	—	18	23	BILF, BILTP

MD = memory disturbance; VSD = visuospatial disturbance; WFD = word finding difficulty; AC = acalculia; LOI = lack of insight; PC = personality change; np = not performed; IM = impossible due to lack of understanding; Bil = bilateral; R = right; L = left; TP = temporoparietal lesion.

Lamoureux et al. (8) constructed quantitative uptake maps of cortical CBF, "CORT-EX", which enable examination of the whole surface cortical perfusion in one image. None of these circumferential displays, however, offer realistic three-dimensional information. Thus, the identification of anatomical structures is difficult unless they have some landmarks in them. With the three-dimensional display, perfusion is displayed as a life-like image and rough anatomical identification is rapid. The circumferential methods were divided into two subtypes in view of regions of interest (ROIs) methods. In the first subtype, the ROIs were drawn as the shape of lobe or the space between concentric circles. In these methods, the cortical values were evaluated by the accumulation of the total region from deep to surface. Methods of this type were considered to be volume evaluation, in which the product of the volume and the rCBF was estimated. In the second subtype, the cortical values were extracted as the maximum of the region. This study used the latter method because the effect of variations on cortical thickness could be minimized. In our method, the mean of the neighboring three values, including the maximum value, was regarded as the corresponding cortical value. Thus, this method takes the ROI in the shape of a closed line along the marginal ridge with a constant width of 6 mm. If the width of the ROI is too narrow, statistical error will be increased due to the lower total counts in the ROIs and if it is too wide, cortical perfusion will be underestimated by partial volume effect and the spatial resolution will decrease. We selected a width of 6 mm as a compromise between these two effects.

To distinguish Alzheimer's disease from other diseases resulting in dementia, some authors have proposed pattern analyses of perfusion in comparison with control individuals. Most of them used normalizing data by a reference value, such as the cerebellum or the occipital cortex (11). The cerebellum is spared in most of Alzheimer's cases

(12). We thus selected the cerebellum as a reference area and defined that less than 60% accumulation in it represented abnormal low perfusion.

In the normal studies, no lesions were demonstrated to be abnormal, except small spotty lesions in two patients. In the study of patients with Alzheimer's disease, TP lesions had abnormal low perfusion in all patients and frontal involvement in six patients, and each lesion was corresponded to a neurological deficit. These low perfusion lesions in Alzheimer's disease agreed with previous reports (13,14) and were easily distinguishable from the spotty lesions of Group C. The accumulation of ^{99m}Tc- HMPAO is not linearly increased in proportion to rCBF (15). To correct this, Lassen et al. (15) proposed a linearization algorithm where blood flow in reference areas was assumed to be constant. The cerebellum, occipital or whole slices were selected as references. Using Lassen's method with the cerebellum as a reference (55 ml/100 ml/min) and 1.5 as the correction constant alpha, the threshold, 60% accumulation of the cerebellum, corresponded to about 25 ml/100 ml/min. This value agreed with a previously reported symptomatic threshold of rCBF reported (16,17). In some individuals, low perfusion was somewhat narrower than expected from their neurological deficits. In these patients, bilateral TP lesions had relatively low accumulation compared with primary sensorimotor areas. The characteristic profile of Alzheimer's disease can be seen in both lateral views. The absolute values of these areas might account for the neurological deficits. This inconsistency may limit these analyses based on perfusion maps and the cerebellum as a reference area. The three-dimensional method is most useful; other cortical regions can be rapidly compared. Difficulty in evaluating perfusion of the most superior portions of the brain is a drawback because of distortion in this area. This limitation, however, may be negligible for most clinical applications.

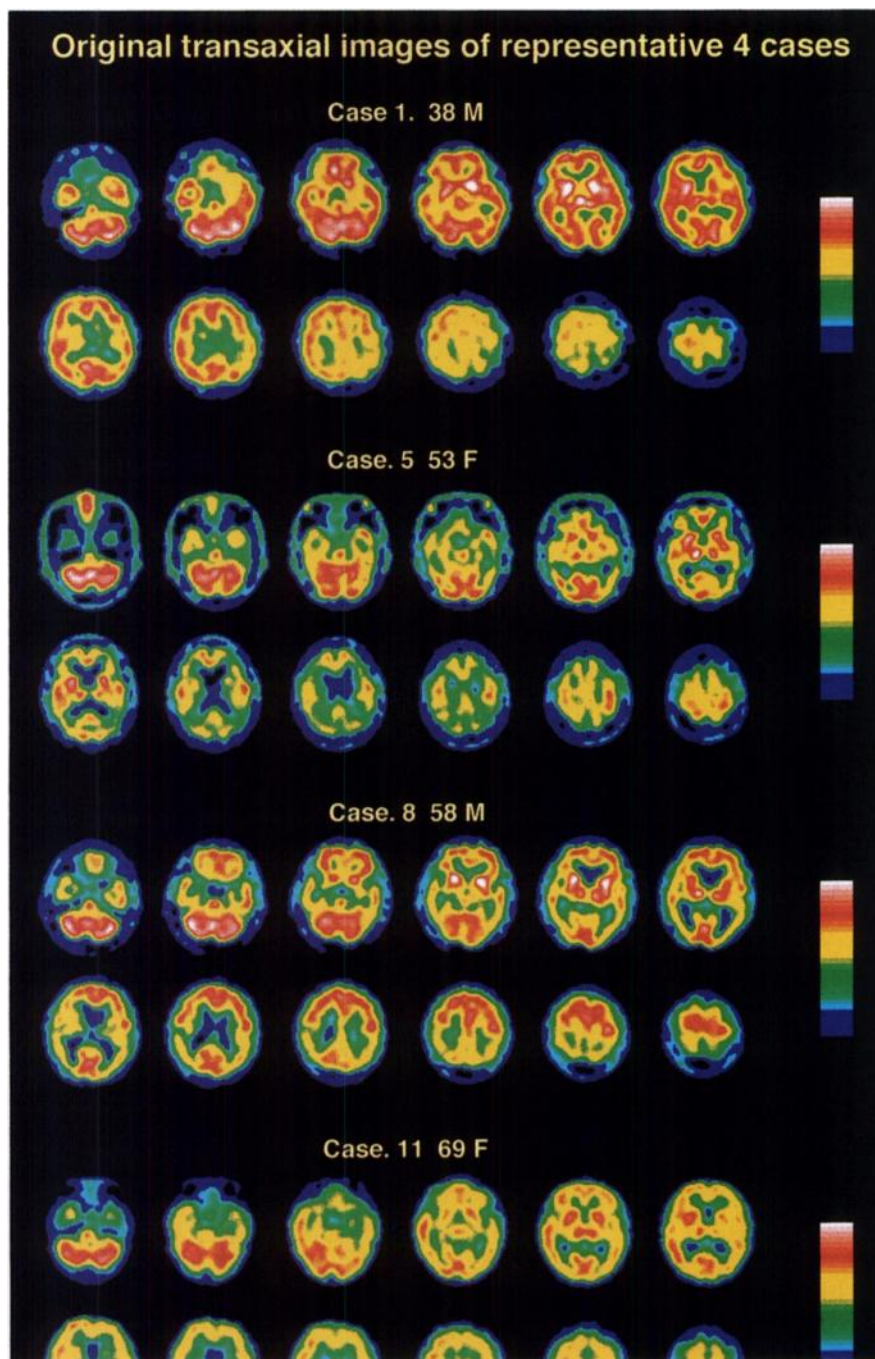


FIGURE 5. The transaxial images of representative patients in Group A. Low perfusion areas can be seen in the transaxial images of patients as well as in the three-dimensional-CBF images in Figure 3. However, three-dimensional-CBF images (Fig. 4) offer the topologically three-dimensional information much easily and quickly than transaxial images.

CONCLUSIONS

This three-dimensional display method provides an overview of cortical surface perfusion obtained by SPECT and enhances the perception of spatial relationships. In Alzheimer's disease, abnormally low perfused areas were demonstrated, which are compatible with neurological deficits. This method may be useful in the diagnosis and follow-up of patients with dementia or cerebrovascular disease.

ACKNOWLEDGMENTS

The authors thank Norifumi Yamada, MD (Department of Neuropsychiatry) for his advice about neurological evaluation; Mr. Takatoshi Maruyama (Hitachi Medical Corporation) for his excellent technical assistance; Ms. Mizuki Tsunoda and Ms. Megumi Shimomura for secretarial assistance.

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