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Color Functional Images of the Cerebral Blood Flow

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Functional gamma imaging, in color, was established for regional cerebral blood flow (rCBF) using ^{133}Xe. During 10 min after intracarotid injection of ^{133}Xe in saline, 60 picture frames of the ^{133}Xe clearance curve for the entire hemisphere were obtained. After nine-point smoothing, the rCBF for each of the 4,096 picture elements was calculated by two methods: the half-time method and the height-over-area method. Both the ^{133}Xe clearance half-times and the calculated CBF values were displayed, using 13 steps of color, as functional CBF images of the brain. Images of peak count and total count were also displayed on the same frame of the color television. Forty-six studies, performed on 37 patients with various cerebral disorders, were divided into two types: diffuse and focal. In the diffuse type, a decrease in CBF was noted in cases of normal-pressure hydrocephalus; successful ventriculoperitoneal shunt operations were followed by recovery of CBF. Occlusion of the middle cerebral artery showed up as a wedge-shaped area of decreased CBF, even when the conventional brain scan looked normal. Increased perfusion to a tumor was frequently associated with decreased CBF in the rest of the lateral hemisphere; such a decrease could be improved by surgical removal of the tumor.

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Using freely diffusible gamma-emitting nuclides, the regional cerebral blood flow (rCBF) has been studied by external monitoring (*1–4*), but with conventional techniques rather few regions of interest in the brain can be studied and the selections are often highly subjective. Recently maps showing rCBF throughout an entire hemisphere (i.e., "functional images") have been generated by computer from quantitative serial images showing the clearance of ^{133}Xe from the brain.*

In the present study, the functional images were made based on clearance curves for ^{133}Xe. Unlike the conventional approach, with its limited number of regions of interest and manual calculation of rCBF, our method allows us to assess the rCBF over the entire hemisphere by a completely automatic setting of regions of interest and to calculate rCBFs by objective means. The final functional images are displayed using 13 color steps. Such a display gives the physician an easily interpretable functional image of the entire cerebral hemisphere. The information would be difficult to read if presented in a gray-scale or numerical form (*5,6*).

The purposes of the present study are to describe the technique for generating functional images for the cerebral blood circulation and to evaluate the practical usefulness of the colored functional images.

METHOD

A scintillation camera with a 140-keV high-sensitivity collimator was connected on-line with the computer. The latter system consisted of a central processing unit† with 24K memory, magnetic disk, magnetic tape, graphic display terminal, and color-television display (Fig. 1).

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Images were obtained successively for 10 min at 10-sec intervals on the left and/or right hemispheres after an intracarotid injection of 10 mCi of ^{133}Xe in saline solution. The image format used 64 × 64 picture elements, each of which corresponded to a 4 × 4-mm area of the actual cerebral hemisphere. The original data were stored on a magnetic disk through the analog-to-digital convertor and the central processing unit using direct memory access. These data were processed in accordance with the flow chart shown in Fig. 2.

After the nine-point smoothing of each image, a ^{133}Xe clearance curve was obtained for each matrix point. The peak count (PC) and peak time (PT) were searched out on these curves. Then the counts in each picture element were summed from peak time to 600 sec to give the total count (TC). Regional cerebral blood flow was calculated by two methods: the half-time (HT) method and the height-over-area method.

In order to obtain accurate half-times, these were calculated using the proportional coefficient method:

$$HT = T_2 - (T_2 - T_1)\left[\frac{\log(PC/2) - \log P_2}{\log P_1 - \log P_2}\right].$$

Here P_1, for any picture element, is the minimum observed count over the value $0.5(PC + W\sqrt{PC})$, where W is a statistical weighting factor, taken as ⅓ in the present study, and P_2, calculated for the same picture element, is the maximum observed count under $0.5(PC - W\sqrt{PC})$. The times corresponding to observed count P_1 and P_2 are designated as T_1 and T_2, respectively. The error due to this method is estimated to be less than 10%. In the half-time method, computed half-times are read out for the color display instead of actual blood flow. The estimated rCBF can be obtained by the following formula:

$$rCBF = 100\lambda\left[\frac{\log 2}{HT}\right].$$

Alternatively, the total area (S) is obtained by adding TC to a count calculated by integrating the ex-

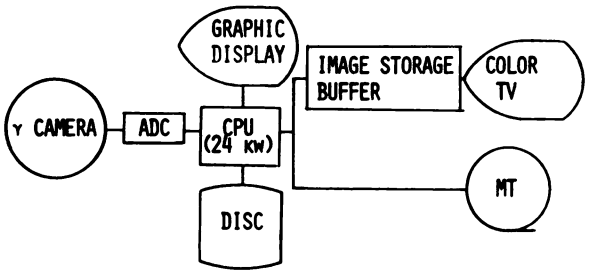


FIG. 1. Block diagram of computer system used in this study.

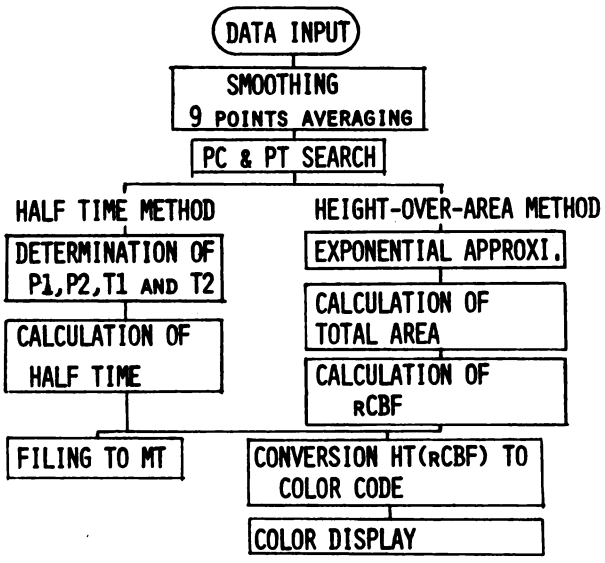


FIG. 2. Flow chart for generating four kinds of colored functional images.

TABLE 1. RELATIONSHIP BETWEEN COLORS AND CBF BY THE HALF-TIME METHOD

Colors	HT (sec)	CBF (ml/min per 100 gm)
Blue	≤40	≥88
Cerulean blue	40–50	71–88
Light green	50–60	59–71
Gray	60–70	50–59
Green	70–80	44–50
Olive	80–90	39–44
Orange	90–100	35–39
Yellow	100–110	32–35
Charcoal gray	110–120	29–32
Brown	120–130	27–29
Red	130–140	25–27
Magenta	140–150	23–25
Violet	150–160	22–23
Black	>160	<22

TABLE 2. BREAKDOWN OF PATIENTS STUDIED FOR REGIONAL CEREBRAL BLOOD FLOW

Diagnosis	No. of studies	No. of patients
Normal-pressure hydrocephalus	10	6
Brain tumor	10	9
Cerebrovascular disease	8	7
Subdural hematoma	9	6
Aneurysm	4	4
Subarachnoidal hemorrhage	1	1
Arteriovenous malformation	1	1
Alzheimer's disease	1	1
Headache	2	2
Total	46	37

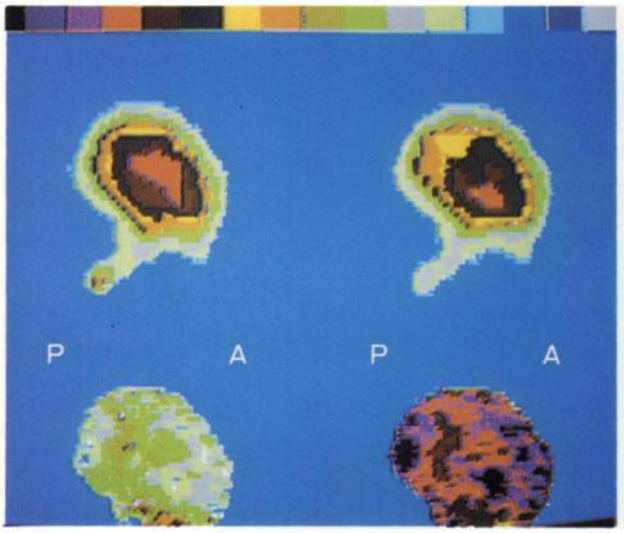


FIG. 3. Functional images of regional cerebral blood flow in normal subject (Case 1). Upper left: total-count image. Upper right: peak-count image. Lower left: half-time image. Lower right: rCBF calculated by height-over-area method.

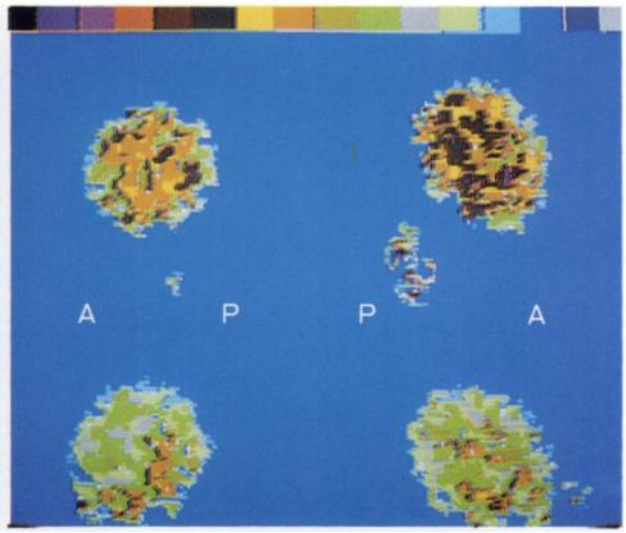


FIG. 4. Half-time images from patient with normal-pressure hydrocephalus before and after ventriculoperitoneal shunt operation (Case 2). Left: Left hemisphere before (top) and after (bottom) operation. Right: Right hemisphere before (top) and after (bottom) operation.

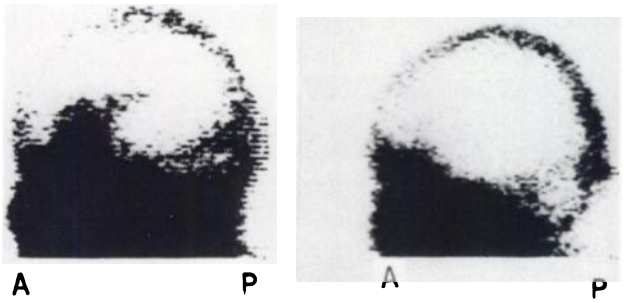
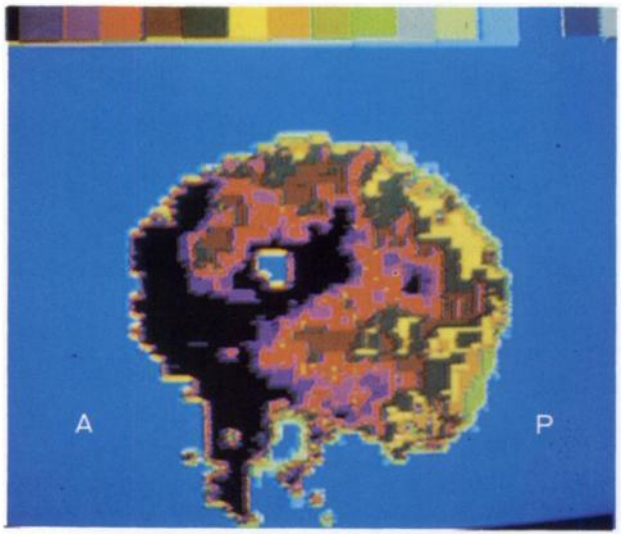


FIG. 5. Brain scans and half-time image in patient with cerebral infarction in distribution of left middle cerebral artery (Case 3). (Above) Brain scans performed 2 weeks (left) and 4 weeks (right) after attack. (Right) Half-time image obtained 4 weeks after attack.



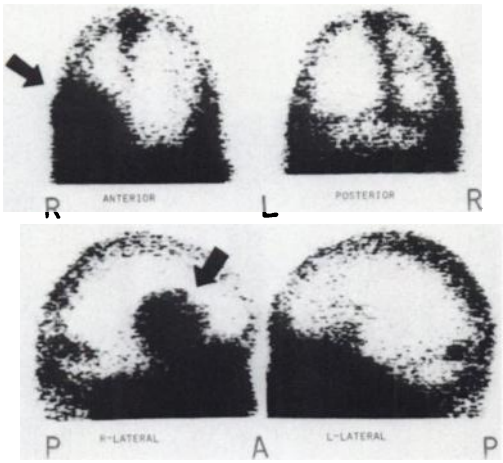
ponential function from 600 sec to infinity. The exponential function is estimated from the tail part of the clearance curves by the least-squares method. The rCBF by the height-over-area method is obtained from PC and S as follows:

$$\text{rCBF} = 100\lambda\left[\frac{\text{PC}}{\text{S}}\right].$$

The coefficient is assumed to equal 0.85 for the half-time method and 1.15 for the height-over-area method.

Values of peak count, total count, half-time, and rCBF by the height-over-area method were calculated for each hemisphere and displayed in color. The peak-count and total-count images were generated with ten steps of color (from cerulean blue to red) covering the range from minimum to maximum. The images depicting rCBF obtained by the height-over-area method were displayed with 13 steps of color from cerulean blue to black; the color steps are linear, each representing 5 ml/min per 100 gm of tissue. The color codings are listed in Table 1. Each color step in the half-time image corresponds to a 10-sec interval, and the corresponding (nonlinear) steps for rCBF (by the HT method) are shown.

All indices of cerebral hemodynamics were proc-



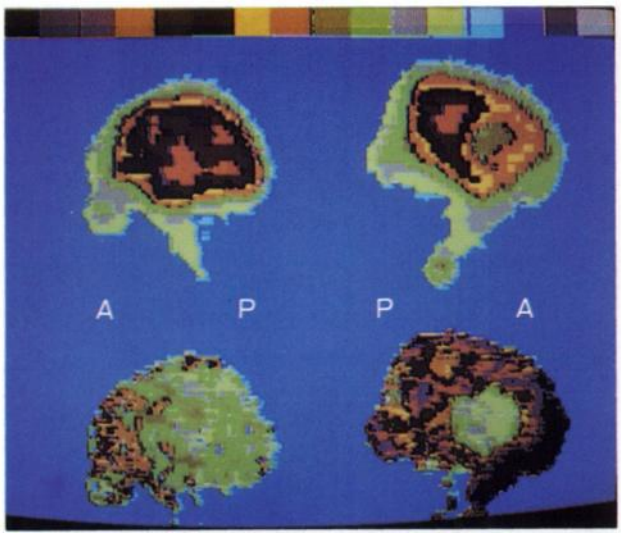


FIG. 6. Brain scans and color functional images of both hemispheres in patient with meningioma (Case 4). (Top) Anterior (upper left), posterior (upper right), right lateral (lower left) and left lateral (lower right) projections of brain scan. Arrows indicate tumor area. (Bottom) Total-count images (upper) and half-time images (lower) of left (left side) and right (right side) hemispheres. See text for details.

essed at the same time. As a final result, the four kinds of reconstructed images were displayed in one frame of a 20-in. color television for each routine study.

Forty-six studies were performed on 37 patients (Table 2). Three out of six patients with normal-pressure hydrocephalus (NPH) were examined before and after a shunt operation. Seven patients were diagnosed as having cerebral vascular disease (CVD), nine had brain tumor, six had subdural hematoma, three had aneurysm, and three patients each had subarachnoidal hemorrhage, arteriovenous malformation, and Alzheimer's disease. Two patients with headaches were also studied.

RESULTS

Functional images of regional cerebral blood flow in a normal subject (Case 1) are shown in Fig. 3. This patient was a 44-year-old woman complaining of headache. Assessments of the right cerebral hemisphere are shown as total-count image, peak-count image, half-time image, and rCBF estimated by the height-over-area method. In the images using peak counts and total counts, the highest count is located at the center of the cerebral hemisphere, with the different color levels forming concentric circles. The normal range of rCBF by the half-time method was calculated to be 40–70 ml/min per 100 gm. Distribution of rCBF was nearly homogeneous, although the estimated blood flow in the peripheral region was higher than that in the other parts of the cerebral hemisphere. The absolute value of rCBF calculated by the HT method was a little larger than that obtained by the height-over-area method, but the rCBF distributions obtained by the two methods were similar, even in the patient with focal brain disease.

Cerebral bloodflow studies were performed before and after a ventriculoperitoneal shunt operation in a 72-year-old woman (Case 2) with NPH (Fig. 4). The average rCBF was 35–45 ml before operation and 45–55 ml after operation, showing significant improvement (*7*). The rCBFs were diffusely distributed throughout both hemispheres. The peak-count and total-count images for this patient showed a concentric pattern like that of a normal subject.

A 67-year-old man (Case 3) with left hemiparesis was studied. A $^{99m}TcO_4^-$ brain scan performed 2 weeks after the attack revealed a large wedge-shaped area of abnormal activity in the distribution of the left middle cerebral artery; it disappeared by the fourth week after the attack (*8*), as shown in Fig. 5 (top). A cerebral bloodflow study was performed for the left cerebral hemisphere of this patient at 4 weeks after the attack. The half-time image revealed a well-demarcated black area in the region of the left middle cerebral artery (Fig. 5, bottom), in spite of the complete disappearance of the hot area in the conventional scan. The arterial blood supply in this area was calculated to be less than 20 ml/min per 100 gm. In the images showing peak count and total count for the same hemisphere, the activity in this region was also decreased.

A 71-year-old man (Case 4) entered the hospital complaining of hand tremor and palpitation. Physical examination revealed no abnormal neurologic signs except tremor. A brain scan, however, revealed a large round high-activity area in the anterior and right lateral views (Fig. 6, top). A carotid arteriogram suggested meningioma. The functional images of the left hemisphere appeared normal, with CBF

values of 40–50 ml/min per 100 gm. In the right hemisphere, however, abnormal distribution of radioactivity was observed in the peak-count and total-count functional images. According to the half-time image, regional blood flow was increased in the tumor area to 60–70 ml/min per 100 gm, while the surrounding parts of the right hemisphere showed a perfusion remarkably depressed to less than 20–30 ml/min per 100 gm.

DISCUSSION

Since Kety and Schmidt first measured the cerebral blood flow using nitrous oxide gas (*9*), the diffusible gaseous radionuclides, such as ^{85}Kr or ^{133}Xe, have been applied as the standard means to assess brain perfusion. Recently, the cerebral dynamic study using a bolus of $^{99m}TcO_4^-$ has also served similar purposes (*10–12*). Although the latter method can be performed easily as a routine procedure, it provides only a rough picture of the cerebral dynamics.

In order to obtain reliable results, it is indispensable to correct for random variations. In the present report, our smoothing of the data was performed not on the clearance curve, but on the original picture elements, using a nine-point averaging method. Smoothing the picture elements is preferred to smoothing the curve because the clearance curve is less rough with the former method than with the latter.

The peak-count and total-count images provide useful general information about brain anatomy and excessive or depleted initial blood supply to any region of the hemisphere. These two functional images normally showed a concentric pattern, while distortion of this pattern occurred in patients with CVD, tumor, or other focal problems. In the patients diagnosed as having an aneurysm, the maximum peak counts were localized at the region of the aneurysm (this is not illustrated in this paper). The total counts at the region of the aneurysm in the same patient were not increased as judged from the total-count images. This fact indicated a large blood volume passing rapidly through this region and suggested such vascular disorders as aneurysm or arteriovenous malformation (*13*).

The half-time method and the height-over-area method adopted here are very simple and do not require a complicated analysis involving several exponentials. Good correlation was found between the two methods, although the absolute value of the rCBF calculated by the HT method is usually larger than that obtained by the height-over-area method. With the HT method, the relationship between the values of the rCBF and the changes of the color is not linear and small changes in rCBF are able to cause color changes when rCBF is low.

The regional functional images of the rCBF can be divided into two types: (A) diffuse perfusion, found in the normal subjects and the patients with NPH, and (B) the focal type, showing a localized area of increased or decreased rCBF, for example, in brain tumor or CVD. The increased blood supply to a discrete brain tumor is probably due to the diversion of arterial blood flow to the tumor, while bloodflow supply to the rest of the hemisphere decreases (Fig. 6). Surgical removal of the tumor resulted in the recovered perfusion of that hemisphere and was associated with alleviation of the senile psychologic symptoms.

Significant increase of the rCBF and improvement of brain function were shown in the cases of NPH after a shunt operation (ventriculoatrial or ventriculoperitoneal). Cerebral infarction is indicated by a wedge-shaped accumulation of $^{99m}TcO_4^-$, seen for a while after the onset of the disease. The scan becomes normal, however, after 6–8 weeks. The perfusion scan with a bolus of $^{99m}TcO_4^-$ has been used to assist in the differential diagnosis of CVD, but often with equivocal results. A ^{133}Xe perfusion scan is of great value not only to detect the occluded area, but also to provide information about regional blood flow. The dynamic brain scan has proved useful in revealing regions of cerebral infarction not visualized with the routine brain scan.

We find that the color display of the entire regional cerebral blood flow gives the physician an improved picture of the cerebral circulation. This cannot be achieved with a monocolor gray-scale display or a simple numerical readout.

FOOTNOTES

* Personal communications from N. A. Lassen and K. Uemura.

† The original program was developed by IBM 1130 in the IBM Scientific Center, Tokyo.

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