Visualization of the Motor Activation Area Using SPECT in Neurosurgical Patients with Lesions Near the Central Sulcus

Yoshihiro Nishiyama, Yuka Yamamoto, Kotaro Fukunaga, Katashi Satoh, Motoomi Ohkawa, Katsuzo Kunishio, and Masatada Tanabe

Departments of Radiology and Neurological Surgery, Kagawa Medical University, Kagawa, Japan

The purpose of this study was to visualize the motor area related to finger movement and a fist-making task using SPECT in patients with lesions near the central sulcus. **Methods:** Eleven patients (9 with a brain tumor, 1 with cerebral infarction, and 1 with an arteriovenous malformation) were investigated. The first intravenous injection of ^{99m}Tc-ethyl cysteinate dimer (ECD) for the motor activation SPECT images was administered 2 min after completion of the fist-making task with the hand contralateral to the brain lesion. The movement was stopped 2 min after injection, and activation SPECT was performed. After the scan, the second dose of ^{99m}Tc-ECD was injected into resting patients, and a second set of SPECT images was acquired. The first set of images was subtracted from the second set to obtain control images. Regions of interest were set bilaterally on the sensorimotor hand area; the supplementary motor area; the frontal, temporal, and occipital lobes; and the cerebellar hemispheres. The results of activation SPECT were expressed as positive or negative for a high-count area, and the regional percentage change for activation images relative to resting images was calculated. **Results:** Visual assessment of activation images was positive in 9 patients for the sensorimotor hand area and 7 patients for the supplementary motor area. The regional percentage change between activation and resting images for the high-count areas was 19.7% for the sensorimotor hand area and 18.2% for the supplementary motor area. Both values were significantly higher than those for other areas ($P < 0.05$). **Conclusion:** Motor activation SPECT using a ^{99m}Tc-ECD split-dose method is easy to perform and may be helpful for presurgical visualization and identification of the sensorimotor hand area or the supplementary motor area.

Key Words: ^{99m}Tc-ECD; SPECT; split-dose method; motor activation; brain mapping

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Preoperative brain mapping is important in patients with lesions of the central nervous system. Activated areas of the brain involved in voluntary movements and visual stimulation must be recognized by measurement of regional cerebral blood flow, regional cerebral oxygen use, and regional cerebral glucose use (*1–3*). By comparing the resting and activation states in each patient, one can identify the brain regions and neural circuits involved in specific cerebral functions (*3–6*).

The recent development of motor activation PET and SPECT has helped to better establish the relationship between clinical functioning and anatomy (*7*). Before activation scanning, the patient performs a behavioral task during injection of radiolabeled tracer. Cerebral perfusion and, therefore, tracer uptake are assumed to be most active in the brain during performance of a task. The use of PET as a reliable and noninvasive preoperative technique for the activation study has been suggested. Nevertheless, this technique is restricted because of its high cost and staff requirements.

^{99m}Tc-ethyl cysteinate dimer (ECD) and ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO) are used clinically as tracers of regional cerebral blood flow (*8*). SPECT is readily available in most large hospitals. With the advent of new tracer ligands (^{99m}Tc-ECD) and resolution-enhancing cameras, SPECT offers the potential for investigation of dynamic brain function across a wide range of clinical and research settings (*9*). However, reports of activation SPECT studies have been only sporadic. The purpose of this study was to use ^{99m}Tc-ECD SPECT to visualize the area related to finger movement in patients with lesions near the central sulcus.

MATERIALS AND METHODS

Patients

We studied 11 patients (3 women, 8 men; age range, 24–78 y; mean age, 54 y), including 3 with a meningioma, 3 with a brain metastasis, 1 with an ependymoma, 2 with an astrocytoma, 1 with a cerebral infarction, and 1 with an arteriovenous malformation. The characteristics of the patients are shown in Table 1. The diagnosis was made by histopathologic examination or by radiologic findings from techniques such as CT, MRI, or angiography. The patients were selected on the basis of their having a lesion near the central sulcus. All patients were right handed. Activation SPECT was performed before intervention. Informed consent was obtained from all patients after a detailed explanation of the study and procedures.

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For correspondence or reprints contact: Yoshihiro Nishiyama, MD, Department of Radiology, Kagawa Medical University, 1750-1 Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0793, Japan.

TABLE 1
Patient Characteristics

Patient no.	Age (y)	Sex	Lesion Type	Location	Size (cm)	Edema	SMHA	SMA
1	69	F	Meningioma	Parietal	3	−	H	H
2	39	M	Meningioma	Parietal	5	−	H	H
3	65	F	Meningioma	Frontal	4	−	H	E
4	67	M	Metastasis	Temporal	2.5	+	H	H
5	47	F	Metastasis	Frontal	2	+	E	H
6	78	F	Metastasis	Frontal	2	+	E	H
7	45	M	Ependymoma	Ventricle	5	−	H	H
8	66	M	Astrocytoma	Temporal	2	−	H	E
9	47	M	Astrocytoma	Parietal	3	−	H	E
10	48	F	Infarction	Parietal	4	−	H	E
11	24	F	AVM	Parietal	1	−	H	H

SMHA = sensorimotor hand area; SMA = supplementary hand area; − = absence; H = hot; E = equivocal; + = presence; AVM = arteriovenous malformation.

Task Design

The task was to make a fist with the hand contralateral to the affected side of the brain. On study entry, each patient was told about the task and asked to try it for a few minutes. The task was performed at a rate of 60 per minute and with the largest possible amplitude, beginning when the examiner touched the opposite hand of the patient and continuing until the examiner again touched the patient's hand. The total time for the task was 4 min.

Imaging Protocol

Activation SPECT was performed using Prism 3000 (Picker International, Cleveland, OH) and high-resolution fan-beam collimators with a spatial resolution of 8 mm full width at half maximum. The projection data were obtained in a 64 × 64 matrix (magnification, ×1.123) for 24 angles at 44 s each over a range of 120°. Image reconstruction was performed using ramp-filtered backprojection. Transverse sections 6.8 mm thick were reconstructed. Scanning was parallel to the orbitomeatal line. Attenuation correction was not performed. A plastic intravenous catheter was inserted into the right antecubital vein 15–30 min before injection. During injection, the patients lay on the imaging table with eyes patched and ears unplugged. The room was quiet, and each patient's head was immobilized in the headrest.

We used a modification of the split-dose activation method and imaging procedure of Takeuchi et al. (*10*) illustrated in Figure 1. The first intravenous injection (370 MBq ^{99m}Tc-ECD) was administered for activation SPECT 2 min after completion of the task. The task was stopped 2 min after injection, and activation SPECT was performed for 17.5 min. After the scanning, the second dose of ^{99m}Tc-ECD (370 MBq × 0.951) was injected for the resting SPECT, and imaging was performed for 17.5 min. Control images were obtained by subtracting the first set of images from the second set.

Data Analysis

Visual Inspection. Activation images were compared with resting images. All images were evaluated visually by 2 radiologists, and the results were classified as positive or negative for a high-count area.

ROI Analysis. For parametric analysis, the regions of interest (ROIs) were drawn with the use of a method described by Oku et al. (*11*) (Fig. 2). On a supraventricular-slice level, the pixel with the highest count around the frontoparietal boundary was identified. The ROI for the sensorimotor hand area (SMHA) was defined as a 20 × 20 mm ROI for which the maximum count was at the center. The mirror-imaged ROI was defined as contralateral SMHA. At the midline of a supraventricular-slice level just anterior to the SMHAs, a 20 × 20 mm ROI was drawn bilaterally to represent the supplementary motor area (SMA). ROIs of the same size were also drawn bilaterally on the cerebellar hemispheres. Elliptical ROIs were drawn bilaterally on the frontal, temporal, and occipital lobes on a midthalamic slice. All ROIs generated during activation SPECT were transferred to the resting images. Seven consecutive sections were selected at and above the level of the thalamus. A whole-section ROI was placed on cortical areas of each of the 7 sections. The mean value in these 7 ROIs was used as an estimate of whole-brain activity (i.e., mean whole-section activity). All ROI counts were normalized to the mean global brain count per pixel. The regional percentage change in normalized counts was calculated as follows: regional percentage change = $C_{task} - C_{cont}/C_{cont} \times 100$, where C_{task} and C_{cont} are normalized mean counts per pixel in the same ROI for activation and resting SPECT, respectively.

Statistical Analysis. The mean regional percentage change was analyzed using Student *t* test. The difference was considered significant when P was <0.05.

RESULTS

The 2 evaluating radiologists correctly identified all lesions on activation and resting images. On activation images, the SMHA was positive in 9/11 patients (81.8%) and the SMA was positive in 7/11 patients (63.6%). In 2 of the 3 patients with a brain metastasis, the SMHA was negative. The regional percentage changes for activation images are shown in Table 2. The percentage change in cerebral perfusion was 19.70% ± 11.45% (mean ± SD) for affected SMHAs, 2.89% ± 4.20% for unaffected SMHAs, and 18.20% ± 16.20% for SMAs. A significant increase in cerebral perfusion occurred in affected SMHAs and SMAs compared with frontal, temporal, and occipital lobes and cerebellum and in affected SMHAs and SMAs compared with unaffected SMHAs ($P < 0.05$). MR and SPECT images of a typical case of meningioma are shown in Figure 3.

DISCUSSION

When the brain is activated, the activity of a population of motor neurons in the cortex correlates closely with regional cerebral blood flow (*1–4*). Therefore, one can visualize the activated parts of the brain by visualizing areas of increased cerebral blood flow.

Several neurofunctional mapping techniques are in use, including PET, SPECT, and functional MRI (*12–15*). Because blood flow and metabolism are coupled in most pathologic states, patterns of abnormality seen on SPECT are similar to those seen on PET for many disorders (*7,9*). PET and functional MRI have the shortcoming of requiring patients to lie on their back during acquisition. SPECT is not influenced by the posture of the patient and can reflect

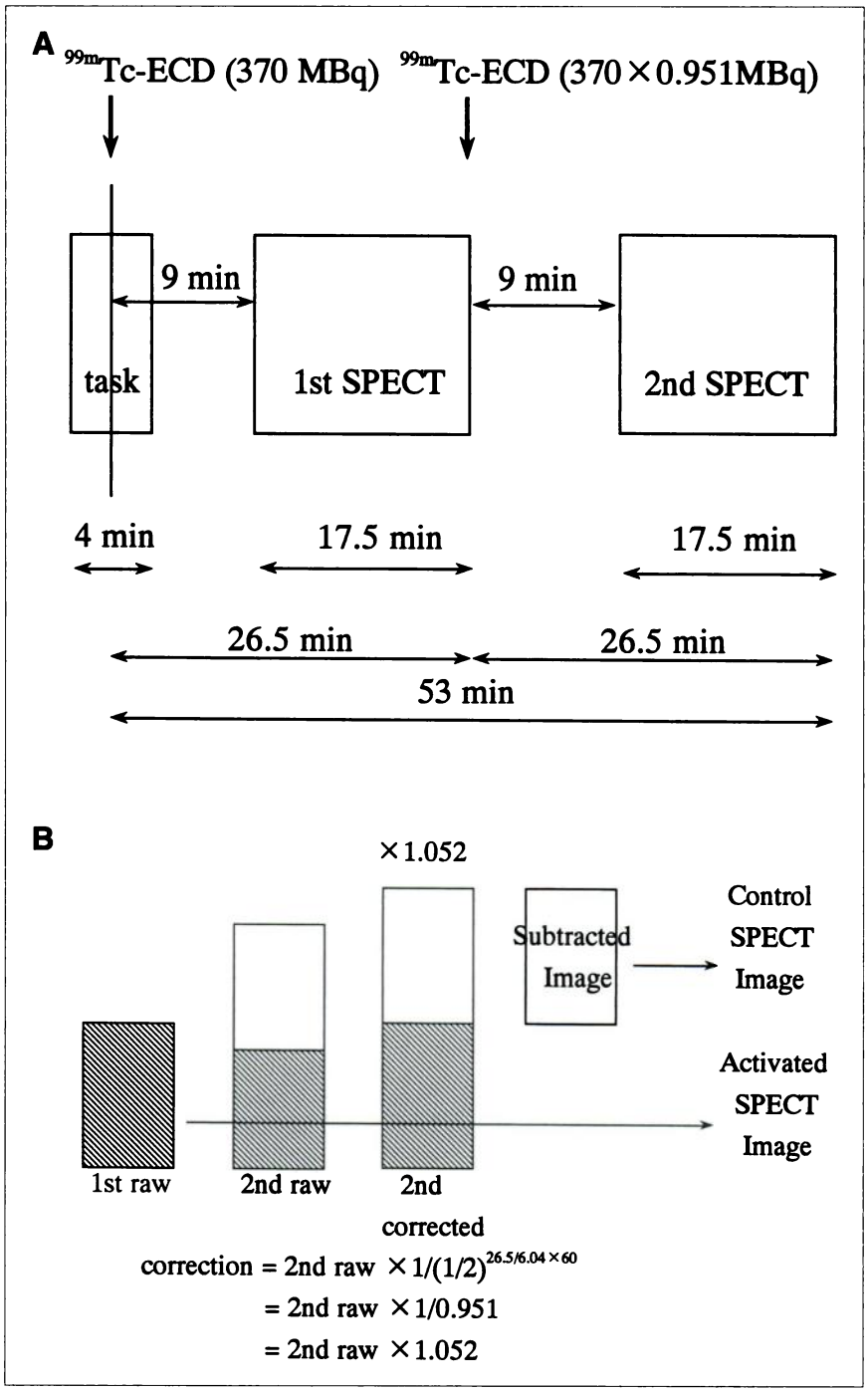

FIGURE 1. Split-dose activation and imaging procedure. (A) Study protocol. Fist-making task was performed for 4 min. First intravenous injection of ^{99m}Tc-ECD was administered 2 min after completion of task. Nine minutes later, first SPECT acquisition was started as activation SPECT. Immediately after acquisition, second injection of ^{99m}Tc-ECD was administered, and second SPECT acquisition was started 9 min later. (B) Image calculation. Control SPECT was calculated by subtracting first SPECT data (1st raw) from second SPECT data (2nd raw) and multiplying by 1.052 (2nd corrected).

cerebral blood flow at the time of radionuclide injection. In this study, 1 methodologic problem was patient movement between the 2 acquisitions. However, we resolved this problem by splitting the dose between the 2 acquisitions and using subtraction. A split-dose method is useful for activation SPECT because SPECT is independent of conditions such as type of task, purpose of study, and posture of patient.

In this study, the first acquisition was activation SPECT. The control images resulted from subtracting the activation images from the resting images and multiplying by a correction factor. This method is the reverse of that described by Sabatini et al. (*16*). The reason for doing so was to prevent head movement of the patient caused by head activation.

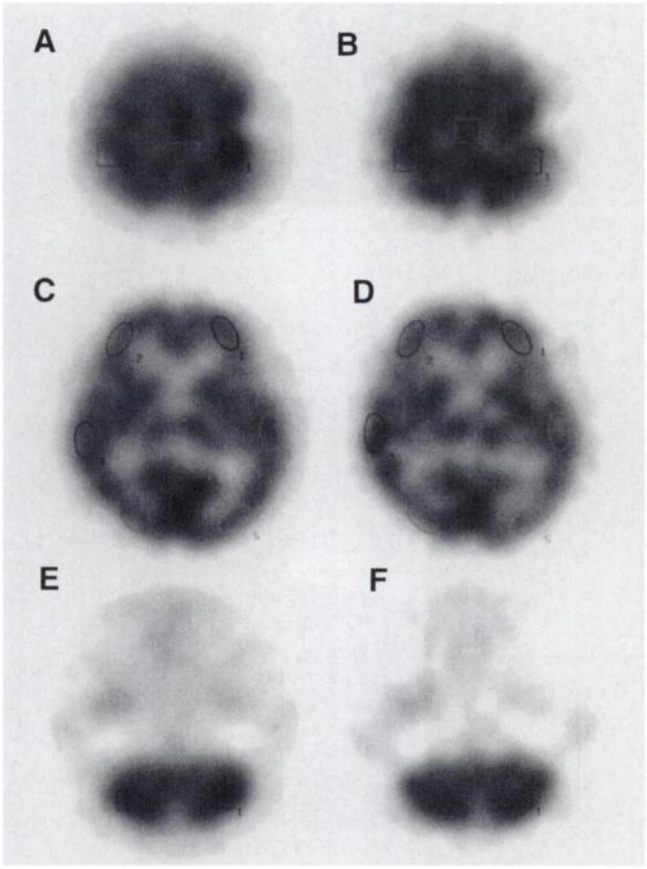

FIGURE 2. Presentation of ROIs on SPECT. Square ROIs for right and left SMHA and SMA were set on supraventricular-slice SPECT image (A, activation; B, control). Elliptical ROIs for bilateral frontal, temporal, and occipital lobes were set on midthalamic-slice SPECT image (C, activation; D, control). Square ROIs for bilateral cerebellar hemispheres were set on SPECT image of cerebellum (E, activation; F, control).

To our knowledge, 4 radioactive tracers have been used in published SPECT neuroactivation studies, including ^{133}Xe, ^{123}I-iodoamphetamine (IMP), ^{99m}Tc-HMPAO, and ^{99m}Tc-ECD (*9,17*). Although first-pass brain extraction is lower for ^{99m}Tc-ECD than for other tracers, ^{99m}Tc-ECD is superior for detecting lesions and contrasting lesions and normal tissues (*8*). More over, for the split-dose method, ^{99m}Tc-ECD has an advantage over ^{99m}Tc-HMPAO in being stable for several hours (*18*).

Although cerebral blood flow imaging agents, such as ^{123}I-IMP, ^{99m}Tc-HMPAO, and ^{99m}Tc-ECD, usually show a defect or decreased uptake in most brain tumors, increased accumulation has sometimes been reported, mostly in hypervascular tumors such as meningiomas or high-grade astrocytomas (*19,20*). ^{123}I-IMP and ^{99m}Tc-HMPAO tend to accumulate in brain tumors more often than does ^{99m}Tc-ECD, which is reported to accumulate in brain tumors only in the early dynamic phase (*19,20*). In this study, SPECT acquisition started 9 min after injection of ^{99m}Tc-ECD. Indeed, the tumors showed decreased perfusion. Therefore, we could discriminate between the lesion and the activated area.

Among the several tasks appropriate for measuring tracer uptake, we selected fist making because it is simple. Sabatini et al. (*16*) reported that regional cerebral blood flow was significantly higher in sensorimotor areas when subjects performed faster, larger-amplitude tasks compared with slower, smaller-amplitude tasks and concluded that activity in the sensorimotor areas depends on the rate and amplitude of stimulation. Fox et al. (*21*) showed that sequential finger-to-thumb opposition performed bilaterally produces symmetric, significant regional cerebral blood flow responses in sensorimotor areas of both the left and the right hemispheres.

The mean regional percentage change on the affected side during the task was 19.7% for the SMHA and 18.2% for SMA. These values are somewhat smaller than those (21%–26%) obtained in some previous studies (*11,22–24*). This difference may be explained, first, by differences between subjects. The previous studies used healthy volunteers, whereas our study included only patients with CNS disease. The patients with brain metastases were believed to have edema surrounding the tumor. A second reason for differences between our findings and those of previous studies may be the low amplitude of stimulation in our study, especially in patients with cerebral infarction. Third, individual variations in the skill with which patients perform complex finger movements may influence the amplitude of the activation area. In addition, Colebatch et al. (*22*) reported increased blood flow in SMAs as well as in SMHAs. In our results, the SMA was positive in 7/11 patients, and all patients with a brain metastasis had a positive SMA.

The most widely used approach for activation studies is measurement of cerebral perfusion with PET or functional MRI (*25*). However, the feasibility of SPECT with perfusion agents for activation studies is not well established. Moreover, locating the activated area in the cortex using this technique is often difficult because of the limited spatial resolution of SPECT images. The solution to this problem

TABLE 2
Regional Percentage Change for Activation Images

ROI	Status or side	Percentage change
SMHA	Affected	19.70 ± 11.45*†
	Unaffected	2.89 ± 4.20
SMA		18.20 ± 16.20*†
Frontal lobe	Right	0.18 ± 3.34
	Left	−3.77 ± 10.30
Temporal lobe	Right	−3.70 ± 17.30
	Left	1.30 ± 4.34
Occipital lobe	Right	−0.25 ± 4.68
	Left	2.36 ± 2.39
Cerebellum	Right	3.31 ± 5.66
	Left	4.58 ± 4.35

*$P < 0.05$ compared with frontal, temporal, and occipital lobes and cerebellum.

†$P < 0.05$ compared with unaffected SMHAs.

Data are mean ± SD.

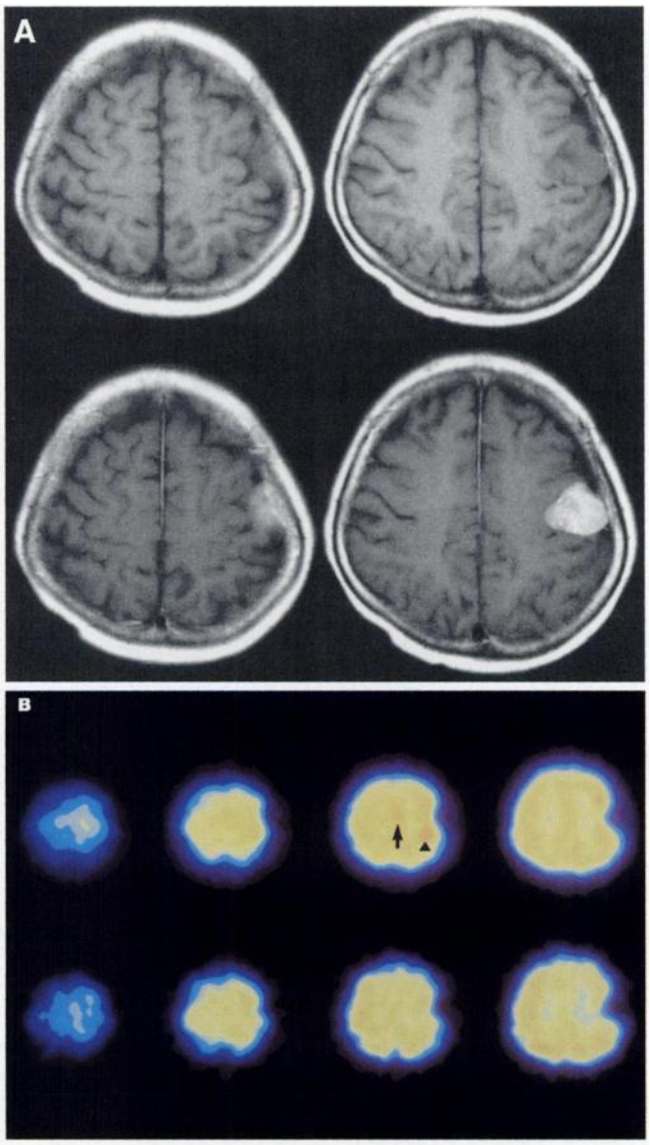

FIGURE 3. MR and SPECT images of 69-y-old woman with meningioma in left parietal lobe. (A) Upper 2 images are unenhanced MR images, and lower 2 are enhanced MR images. Lower images show abnormal enhancement in left parietal lobe. (B) Upper 4 images are activation SPECT, and lower 4 are resting SPECT. Motor task was fist making with right hand. Left SMHA (arrowhead) and SMA (arrow) are clearly visualized as hot spot foci on activation images. Left SMHA and SMA are not observed on resting images. Regional percentage change was 27% for SMHA and 25% for SMA.

may be to superimpose the SPECT images on morphologic images such as CT scans and MR images. Further work such as statistical parametric mapping needs to be added to activation studies.

CONCLUSION

The motor activation SPECT method using a split dose of ^{99m}Tc-ECD is easy to perform. This method of brain mapping may be helpful for visualizing the sensorimotor hand area or the supplementary motor area and for identifying the central sulcus. Thus, this method can be useful for planning neurosurgical treatment in patients with lesions near the central sulcus.

REFERENCES

1. Fox PT, Raichle ME. Stimulus rate dependence of regional cerebral blood flow in human striate cortex, demonstrated by positron emission tomography. *J Neurophysiol.* 1984;51:1109–1120.
2. Wise R, Chollet F, Hadar U, et al. Distribution of cortical neural networks involved in word comprehensive and word retrieval. *Brain.* 1991;114:1803–1817.
3. Matthew E, Hill TC. Brain mapping with single photon emission CT. *Radiology.* 1998;206:483–489.
4. Sokoloff L. Relationships among local function activity, energy metabolism, and blood flow in the central nervous system. *Fed Proc.* 1981;40:2311–2316.
5. Yarowsky PJ, Ingvar DH. Neural activity and energy metabolism. *Fed Proc.* 1981;40:2353–2362.
6. Kosslyn SM, Thompson WL, Kim IJ, Alpert NM. Topographical representations of mental images in primary visual cortex. *Nature.* 1995;378:496–498.
7. Alavi A, Hirsch LJ. Studies of central nervous system disorders with single photon emission computed tomography and positron emission tomography: evolution over the past 2 decades. *Semin Nucl Med.* 1991;11:58–81.
8. Friberg L, Andersen AR, Lassen NA, Holm S, Dam M. Retention of ^{99m}Tc-bicisate in the human brain after intracarotid injection. *J Cereb Blood Flow Metab.* 1994;14(suppl):S19–S27.
9. Ring HA, George M, Costa DC, Ell PJ. The use of cerebral activation procedures with single photon emission tomography. *Eur J Nucl Med.* 1991;18:133–141.
10. Takeuchi R, Matsuda H, Yonekura Y, Sakahara H, Konishi J. Noninvasive quantitative measurements of regional cerebral blood flow using technetium-99m-L,L-ECD SPECT activated with acetazolamide: quantification analysis by equal-volume-split ^{99m}Tc-ECD consecutive SPECT method. *J Cereb Blood Flow Metab.* 1997;17:1020–1032.
11. Oku N, Matsumoto M, Hashikawa K, et al. Super-early iodine-123 iodoamphetamine SPECT imaging of human primary motor cortex. *J Nucl Med.* 1995;36:2180–2185.
12. Woods SW, Hegeman IM, Zubal I, et al. Visual stimulation increases technetium-99m-HMPAO distribution in human visual cortex. *J Nucl Med.* 1991;32:210–215.
13. Ramsey NF, Kirkby BS, Van Gelderen P, et al. Functional mapping of human sensorimotor cortex with 3D BOLD fMRI correlates highly with $H_2{}^{15}O$ PET rCBF. *J Cereb Blood Flow Metab.* 1996;16:755–764.
14. Crosson B, Williamson DJG, Shukla SS, Honeyman JC, Nadeau SE. A technique to localize activation in the human brain with technetium-99m-HMPAO SPECT: a validation study using visual stimulation. *J Nucl Med.* 1994;35:755–763.
15. Votaw JR, Li HH. Analysis of PET neurofunctional mapping studies. *J Cereb Blood Flow Metab.* 1995;15:492–504.
16. Sabatini U, Chollet F, Rascol O, et al. Effect of side and rate of stimulation on cerebral blood flow changes in motor areas during finger movements in humans. *J Cereb Blood Flow Metab.* 1993;4:639–645.
17. Guenther W, Moser E, Mueller-Spahn F, Oefele K, Buell U, Hippius H. Pathological cerebral blood flow during motor function in schizophrenic and endogenous depressed patients. *Biol Psychiatry.* 1986;21:889–899.
18. Walovitch RC, Franceschi M, Picard M, et al. Metabolism of Tc-99m-L,L-ethyl cysteinate dimer in healthy volunteers. *Neuropharmacology.* 1991;30:283–292.
19. Hirano T, Suzuki H, Higuchi T, et al. Grade 2 astrocytoma visualized by technetium-99m ECD SPECT. *J Nucl Med.* 1996;37:273–275.
20. Oshima M, Konoeda K, Karigome M, et al. Evaluation of ^{99m}Tc-ECD SPECT for the detection of brain tumor: comparison with ^{201}TI SPECT. *Nippon Acta Radiol.* 1997;57:52–57.
21. Fox PT, Raichle ME, Burde RM, et al. The role of cerebral cortex in the generation of voluntary saccades: a positron emission tomography study. *J Neurophysiol.* 1985;54:348–369.
22. Colebatch JG, Deiber MP, Passingham RE, Friston KJ, Frackowiak RSJ. Regional cerebral blood flow during voluntary arm and hand movements in human subjects. *J Neurophysiol.* 1991;65:1392–1401.
23. Roland PE, Larsen B, Lassen NA, Skinhoj E. Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J Neurophysiol.* 1980;43:118–136.
24. Ebmeier KP, Murray CL, Dougall NJ, O'Carroll RE, Doodwin GM. Unilateral voluntary hand movement and regional cerebral uptake of technetium-99m-exametazine in human control subjects. *J Nucl Med.* 1992;33:1637–1641.
25. Sadato N, Ibanez V, Campbell G, Deiber MP, Bihan DL, Hallett M. Frequency-dependent changes of regional cerebral blood flow during finger movements: functional MRI compared to PET. *J Cereb Blood Flow Metab.* 1997;17:670–679.