

# Usefulness of $^{99m}\text{Tc}$ -HMPAO SPECT in the Localization of the Epileptic focus in Temporal Lobe Epilepsy: Comparison with EEG, MRI and CT.

**Jong Ho Kim, M.D. and Jong Soon Kim, M.D.**

*Department of Internal Medicine, Han Il Hospital, Seoul, Korea*

**Sang Eun Kim, M.D., Chang Woon Choi, M.D., Dong Soo Lee, M.D.  
June-Key Chung, M.D., Myung Chul Lee, M.D. and Chang-Soon Koh, M.D.**

*Department of Internal Medicine.*

*College of Medicine, Seoul National University, Seoul, Korea.*

**Nam Soo Lee, M.D. and Ho Jin Myung, M.D.**

*Department of Neurology*

＝ 국문 초록 ＝

측두엽성간질의 간질병소 편측화에서  $^{99m}\text{Tc}$ -HMPAO SPECT의 유용성 :  
뇌파, 자기 공명 영상 및 전산화 단층 영상과의 비교.

한일 병원 내과

김 종 호 · 김 종 순

서울대학교 의과대학 내과학교실

김상은 · 최창운 · 이동수 · 정준기 · 이명철 · 고창순

신경과학교실

이 남 수 · 명 호 진

뇌 혈류의 기능적 영상화는 간질병소의 국소화에 이용되고 있으며 측두엽성간질의 편측화에 여러 가지 진단 방법이 이용되고 있으나 만족할만한 결과를 보이지 못하고 있다. 최근 PET 또는 SPECT를 이용하여 측두엽성간질에서 발작 간에 측두엽 병소의 대사율 및 혈류의 감소가 나타나며, 이러한 소견은 발작 유발 병소의 편측화에 매우 유용할 것이라는 보고들이 있다. 저자들은 측두엽성간질에서 간질 병소를 편측화 하는데에  $^{99m}\text{Tc}$ -HMPAO SPECT의 유용성을 평가 하고자 측두엽성간질 31예에서 발작 간의  $^{99m}\text{Tc}$ -HMPAO SPECT 소견, 뇌파, 자기 공명 영상 및 전산화 단층 소견을 비교 하였다.

SPECT 소견에 따른 나이, 병력 기간과 병발시 나이 등의 임상 지수 간에는 유의한 차이가 없었다. 31예의 환자중 23예에서(74.2%) 국소 뇌 혈류 감소를 보였으며 17예(54.8%)에서 측두엽에 관

류 감소가 관찰 되었다. 비인두 뇌파 표준 뇌파는 24예(77.4%)에서 측두엽에 편측화를 보였으며 SPECT와 뇌파 양자가 모두 편측화된 경우 일치도는 8/12예(66.7%) 였다. 16예에서 시행된 전산화 단층 영상은 모두 편측화를 보이지 못했으며 27예에서 시행된 자기 공명 영상에서는 단지 1예에서 편측화를 보였다.

이상의 결과로서 발작 간의  $^{99m}\text{Tc}$ -HMPAO SPECT는 측두엽성간질 병소의 편측화에 유용한 보조 검사로 생각된다.

## INTRODUCTION

Positron emission tomography (PET) has established a place in the lateralisation of a temporal lobe epileptic focus prior to surgery. Interictal studies have suggested that it detects temporal lobe hypoperfusion or hypometabolism in 75% of patients with intractable disease<sup>1-4</sup>. Hyperperfusion or hypermetabolism is detected ictally<sup>2,4,5</sup>.

Single photon emission computed tomography (SPECT) can also image regional cerebral blood flow (rCBF) in focal epilepsy<sup>6,7</sup>, with similar results. While it is a much cheaper and more predictable technique, it has not been widely applied, primarily because of lack of availability of radiochemicals suitable for imaging blood flow.  $^{99m}\text{Tc}$ -hexmethylpropyleneamine oxime ( $^{99m}\text{Tc}$ -HMPAO)<sup>8</sup> allows imaging of regional cerebral blood flow (rCBF) with SPECT, and is now widely available. We have studied 31 patients to determine whether this technique is useful in showing lateralising abnormalities in temporal lobe epilepsy (TLE). The aim of our study was to determine the role of  $^{99m}\text{Tc}$ -HMPAO SPECT imaging in patients with TLE by evaluation of the interictal period. We included only interictal SPECT studies during rest and under normal medication in this study.

## MATERIALS AND METHODS

### 1. Patients

Thirty one patients with known or suspicious TLE were (16 males and 15 females) seen and reviewed

with charts from January, 1989 to January, 1991. Their ages ranged from 9-49 (mean 25.3) years. The length of seizure history ranged from 1-25 (mean 7.9) years and the ages at the onset were from 8-49 (mean 18.4) years.

The inclusion criteria for this study was a definite clinical diagnosis of temporal lobe epilepsy. This required both the absence (stare combined with impaired awareness and responsiveness), and features of temporal lobe involvement in the aura, such as *deja vu*, or in the seizure itself, such as automatism.

### 2. Clinical Parameters

Clinical information was obtained by a combination of patient interview and review of case records. Patients age, length of history of seizure disorder and age of onset were also recorded.

### 3. Scanning Technique

In all 31 patients  $^{99m}\text{Tc}$ -HMPAO SPECT was performed. The patients were injected intravenously with 740 MBq (20 mCi) of Tc-labelled HM-PAO in adults or 370 MBq (10 mCi) in child. They were scanned within 1 hour of injection using a Siemens ZLC-750 ROTA Gamma camera producing 6 mm axial sections parallel to the orbito-meatal line. The in place resolution of this system is 12 mm FWHM, and the images are comparable to those of rCBF obtained by most PET systems currently in use.

The SPECT was interpreted blind to EEG findings but not to the diagnosis of temporal lobe epilepsy.

#### 4. MRI and CT.

In 27 out of 31 patients (87.1%) MRI was carried out. MRI was performed using a 2.0 T scanner (Superconduct 20000) or a 0.5 T scanner (Supertec 5000), producing axial proton density images (TR/TE=2500 msec/30 msec) and T2 weighted images (500/30) by spin echo technique.

In 14 out of 31 patients (45.2%) CT was performed. CT was carried out using a General Electrics 9800 Tomoscan, producing axial 10 mm sections of the whole brain, after 50-100 ml (300 mg/ml iodine) of intravenous contrast medium.

MR and CT images were interpreted and reported independently by two investigators, blind to any data other than the diagnosis of temporal lobe epilepsy. Disagreements between reports were resolved by *consensus conference*.

#### 5. EEG

In all 31 patients multiple sleep-deprived nasopharyngeal EEG with standard international 10-20 system electrode placement was done.

### RESULTS

Data pertaining to the 31 patients in the temporal lobe epilepsy are summarized in the Table 1. All patients were studied in interictal state and under normal medication.

The patients were divided into 3 groups (Table 2), those with normal rCBF patterns, those with hypoperfusion in temporal lobe and those with rCBF abnormalities outside the temporal lobe (nonspecific). These groups were compared in terms of age, length of history and age at onset of epilepsy. All the parameters had a wide range in both groups and none of the differences between them was statistically significant. Late onset of disease was commoner in the nonspecific group, however this difference just failed to reach statistical significance.

#### 1. SPECT

The HM-PAO SPECT images of 23 of the 31 patients (74.2%) showed abnormalities in the regional brain perfusion. In 17 out of 31 cases (54.8%) unilateral temporal hypoperfusion was seen, two on the right, 10 on the left, and five on the bilaterally confined to, or involving temporal lobe. Eight patients (25.8%) had a normal perfusion pattern. Six patients (19.4%) had nonspecific rCBF abnormalities outside the temporal lobe (Table 3, 4, 5, 6 )

#### 2. MRI

Cerebral MR examinations were carried out in 27 out of 31 patients (87.1%). In 3 cases focal changes were found. MRI detected a specific lateralising abnormality in only one patient, a small area of sclerosis in the temporal lobe in which were in the same position as shown by the perfusion disturbances demonstrated in SPECT, and the focus indicated by EEG. In the other two cases, circumscribed structures with different signal intensities were seen outside the temporal lobe, in which the MR and SPECT images closely corresponded. Magnetic resonance of 24 patients failed to reveal any abnormalities (Table 3, 4).

#### 3. CT

Cranial CT examinations were performed in 16 out of 31 patients (51.6%). The CT of 16 patients detected no specific lateralising abnormality. In the two cases nonspecific abnormalities were present. The one patient exhibited diffuse atrophy, although the symptoms of the seizures had not indicated that they had originated from these areas. Comparison of the EEG findings with these of the HM-PAO SPECT images had not shown a correlation in this case. The other patient exhibited the low density of the left occipital area nonspecifically with hypoperfusion in the SPECT. 14 patients had normal CT findings

Table 1. MR, CT, EEG, and SPECT Findings in the Individual Patients

Case no/sex/age	MR 1. localization 2. appearance signal intensity	CT 1. localization 2. appearance density	EEG localization	SPECT (rCBF) localization
1/23/M	(L) 0 HSI	(L) 0 low density	(L) F-T	(L) T (L) P-O
2/21/M	normal	normal	(L) T	(L) T (R) BG
3/19/M	normal		(L) F-T	(L) T
4/17/M	normal		(L) T	(L) T
5/34/M	normal	normal	(L) F-T	(L) F-P-T
6/34/F	normal	normal	(R) F-T	(R) T
7/12/F		normal	(L) F-T (R) F-T	(L) F-P-T (R) P-T
8/ 9/F	normal		(L) F-T (B) F	(B) T
9/22/M	normal	normal	(L) T	(L) T (R) F-T (L) BG
10/23/F	normal	normal	(R) P-T	(B) T
11/20/M	(L) T sclerosis		(B) F-T	(L) F-P-T
12/35/F	normal		(R) T	(L) T
13/49/M		diffuse atrophy	normal	(L) T
14/33/M	normal		normal	(L) F-P-T (L) BG (B) cbl
15/22/M	(R) Cbl HSI	normal	(R) P	(L) T (R) cbl
16/13/M			(R) F	(R) T
17/17/F	normal		normal	(L) F-P-T (R) F-T (R) BG, (B) Thal
18/72/F		normal	(L) F-T	normal
19/13/F	normal	normal	(L) T-O	normal
20/18/F		normal	(L) T	normal
21/23/F	normal		(R) F-T	normal
22/20/F	normal		(R) F-T	normal
23/32/M	normal		(R) F-T	normal
24/20/F	normal	normal	(R) F-T (L) T	normal
25/43/F	normal		(B) F-T	normal
26/35/F	normal		(L) T	(R) F
27/15/F	normal	normal	(R) F-T	(R) BG
28/48/M	normal	normal	(R) F-T	(L) F
29/40/M	normal		(L) F-T (R) F-T	(L) P-O (R) P
30/15/M	normal	normal	normal	(L) Thal
31/28/M	normal		normal	(L) F

(L) : left, (R) : right, (B) : bilateral,  
F : frontal, P : parietal, T : temporal, O : occipital, BG : basal ganglia, Cbl : cerebellum, Thal : thalamus,  
HSI : high signal intensity

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Table 2. Clinical Parameters

	Whole group (n=31)	Normal SPECT (n=8)	Hypoperfusion in Temporal (n=17)	Nonspecific (n=6)
Age (years)	25.32 ± 10.73	31.38 ± 17.90*	23.71 ± 9.92*	22.67 ± 10.70*
Length of history (years)	7.87 ± 6.35	10.50 ± 6.50**	6.47 ± 4.33**	8.33 ± 8.79**
Age of onset (years)	18.42 ± 10.32	15.63 ± 6.82#	18.24 ± 10.76#	30.17 ± 12.27#

Values = mean ± S.D. (standard deviation) \* : p > 0.05, \*\* : p > 0.05, # : p > 0.05.  
Nonspecific : rCBF abnormalities outside the temporal lobe.

Table 3. Summary of Results of MRI, CT, EEG and SPECT

	CT	MRI	SPECT	EEG
Normal	14	24	8	5
Unilateral temporal abnormalities	0	1	12	19
Bilateral temporal abnormalities	0	0	5	5
Nonspecific	2	2	6	2
Total	16	27	31	31

Nonspecific ; rCBF abnormalities outside the temporal lobe.

Table 4. TLE : Percentage of Cases Showing Lateralising Lesion on SPECT, MR, CT and EEG of 31 Patients with TLE

	MR n=27	CT n=14	SPECT n=31	EEG n=31
TLE n=31	1 (3.7%)	0 (0.8%)	17 (54.8%)	24 (77.4%)

(Table 3, 4).

#### 4. EEG

Multiple surface EEG recordings were done in all 31 patients. 26 of the 31 patients (83.9%) showed EEG abnormalities. In 24 out of 31 patients (77.4%) EEG showed an epileptogenic focus. In 11 cases both the focus indicated by the EEG and the SPECT findings were on the same side. The location was consistent in 8 cases (correlation rate=66.7%). In only one patient EEG abnormalities was accompanied by contralateral temporal hypoperfusion in SPECT.

Table 5. Summary of SPECT Findings in 31 Patients with TLE

Normal	8
Lateralizing lesion	17
	Unilateral 12 Bilateral 5
Nonspecific	6
Total	31

Nonspecific ; rCBF abnormalities outside the temporal lobe

Table 6. Correlation of Lateralisation in HMPAO/SPECT and EEG in 31 Patients (Number of cases)

		SPECT			N	ns	
		(L)	(R)	(B)			
EEG	(L)	5		1	3	1	10
	(R)	1	1	1	3	2	8
	(B)	1		2	2	1	6
	N	2		1		2	5
	ns	1	1				2
		10	2	5	8	6	31

(L) : left, (R) : right, (B) : bilateral,

N : normal, ns : nonspecific rCBF abnormalities outside the temporal lobe

The two of the 31 patients showed signs of multifocal increased excitability or slight nonspecific abnormalities. Electroencephalography of five of the 31 patients showed no abnormalities (Table 3, 4, 6).

### 5. Comparison of SPECT with CT and MRI (comparison of “functional” with “structural” scans)

SPECT detected abnormalities in 17 patients in whom CT and MRI were normal or showed only anatomical asymmetry. In 12 of these patients the abnormalities were unilateral and in five bilateral. In one case lateralising abnormalities were seen on MRI. There were no cases where CT or MRI showed a definite lesion on one side and SPECT lateralized

to the other (Table 3, 4) (Fig. 1, 2, 3).

### 6. Correlation of SPECT with MRI and/or CT, with Surface EEG

Multiple surface EEG recordings gave consistent lateralisation in 24 patients. There were lateralising abnormalities on SPECT with MRI and/or CT in 17 of these patients. Where SPECT and EEG recordings were both lateralising, agreement between them was good, in 8 out of 12 cases (correlation rate=66.7%). In only one patient temporal hypoperfusion in

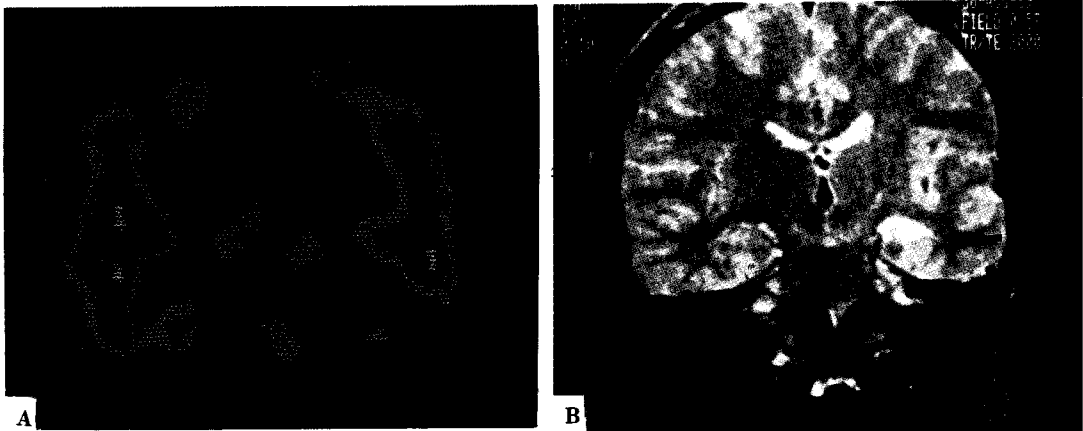


Fig. 1. A 20-year-old male patient with the temporal lobe epilepsy; EEG focus in the bilateral temporal lobe.  
1-A: SPECT image shows reduced regional cerebral blood flow of the left temporal lobe.  
1-B: MR image shows the left temporal sclerosis (high signal intensity) (arrow).

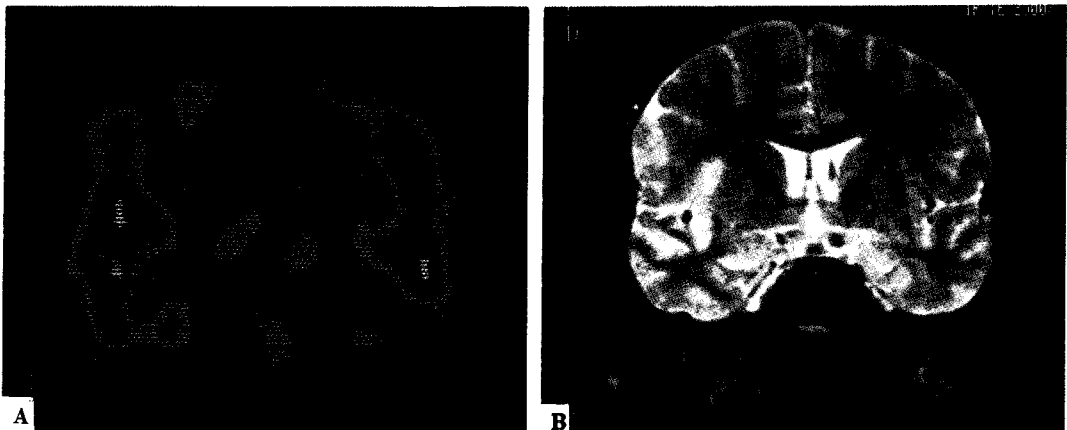
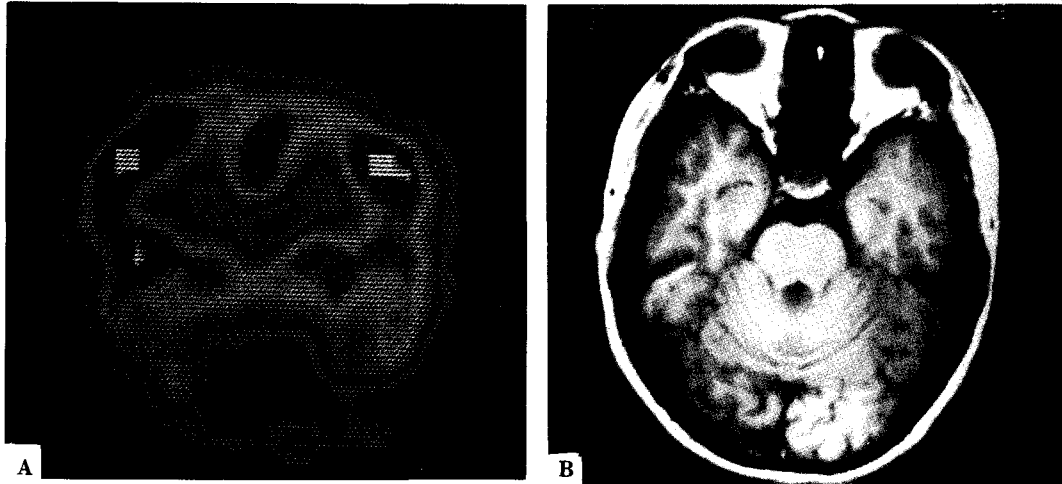


Fig. 2. A 21-year-old male patient with the temporal lobe epilepsy; EEG focus in the left temporal lobe.  
2-A: SPECT image reveals reduced regional cerebral blood flow of the left temporal lobe.  
2-B: MR image fails to demonstrate any focal lesion.



**Fig. 3.** A 25-year-old female patient with the temporal lobe epilepsy; EEG focus in the bilateral temporal lobe.  
3-A: SPECT image reveals reduced regional cerebral blood flow of the bilateral temporal lobe.  
3-B: MR image fails to demonstrate any focal lesion.

SPECT was accompanied by contralateral EEG abnormalities (Table 6).

## DISCUSSION

Brain blood flow disturbances in the seizure disorders have been recognized for many years. In 1968, Plum et al<sup>10)</sup> described elevation of mean brain blood flow during seizures induced in experimental animals. Ingvar,<sup>11)</sup> using intra-arterially injected  $^{133}\text{Xe}$  and a scintillation multiprobe system, measured surface regional brain blood flow with a wash out technique, and observed that during a seizure there was locally increased brain blood flow in the probable location of the seizure focus, while during the interictal period, flow in the focal region was often subnormal. Kuhl and associates<sup>12)</sup>, applying positron emission tomographic (PET) imaging to the study of rCBF and regional brain glucose metabolism, have produced three-dimensional maps of abnormal blood flow and metabolism resulting from seizure disorders. Elevated flow and glucose metabolism have been seen in seizure foci, together with interictal ischemia and reduced metabolism.

HM-PAO is a lipophilic oxime. It crosses the blood brain barrier freely, and 85% of brain uptake occurs on the first pass after an intravenous injection. Once inside brain tissue, it forms a hydrophilic compound. This can slowly recross the blood brain barrier, and so its pattern of distribution in the brain, and that of the technetium 99 m with which it is labelled, reflects the amount delivered and hence rCBF at the time of the first pass after intravenous injection. The activity in brain tissue remains essentially constant for several hours (3), allowing a delay before scanning. Since rCBF correlates closely with regional cerebral metabolism in epilepsy<sup>5,14)</sup>, HM-PAO SPECT effectively images both. Several reports have shown the superiority of MRI over CT in detecting lateralising lesions in temporal lobe epilepsy<sup>13-18)</sup>. It is difficult to make direct comparison in terms of the abnormality rate, but most studies show an MRI abnormality rate of 20~25% in patients with normal CT<sup>13-16)</sup>.

Interictal studies in temporal lobe epilepsy using both positron emission tomography (PET) and SPECT have found focal temporal hypoperfusion as the most common abnormality<sup>19,20)</sup>. Their detection is

important, as bilateral abnormalities of rCBF must be regarded as representing at least a relative contraindication to surgery. Surgical treatment appears to be useful in patients with intractable seizures. When patients are considered candidates for surgical intervention, however, all risks associated with the procedure should be well-known and estimated as precisely as possible. Prior to surgery, all available diagnostic tools must be utilized to identify the focus. Positron emission tomography (PET) and SPECT using tracers for metabolism, blood flow and benzodiazepine-receptors are nuclear medicine approaches that have proven useful for identification of such foci<sup>21~24</sup>). Circumscribed ictal hyperperfusion/hypermetabolism and interictal hypoperfusion/hypometabolism represents the classic constellation for the epileptic focus, although (particularly ictally) additional regional cerebral blood flow changes occur distant from the epileptic focus<sup>25~29</sup>).

The correlation between lateralisation based on single surface EEG recording and that based on hypoperfusion seen on PET or SPECT is poor, but improves as the results of multiple recordings are taken into account and becomes very good when the results of all EEG investigations, including depth electrodes etc, are taken into account<sup>30</sup>). Other authors report correlations of interictal SPECT and EEG between 28%<sup>31</sup>) and 95%<sup>32</sup>). Bonte et al<sup>33</sup>) observed abnormal SPECT studies using xenon-133 in 36 out of 74 patients with partial seizures in the absence of organic lesions, In 28 cases, localization agreed with the interictal EEG. Cordes et al<sup>34,35</sup>) reported agreement of SPECT and EEG in 20 of 47 patients with temporal lobe epilepsy

Although the EEG investigations of our patients were largely based on sleep-deprived nasopharyngeal EEG with standard international 10~20 system electrode placement, the correlation with SPECT was good (correlation rate=66.7%). Localization within the temporal lobe is not always possible using inter-

ictal PET or SPECT. The results of this study show that low field MRI is superior to modified CT in detecting abnormalities of the temporal lobe and suggest that SPECT should become part of the standard workup for the evaluation of lateralisation of the temporal lobe epilepsy, especially in the medically intractable TLE preoperatively. Further investigations of the ictal EEG monitoring including depth electrode neuroreceptor study and ictal SPECT should be considered.

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