Ictal and Interictal Technetium-99m-Bicisate Brain SPECT in Children with Refractory Epilepsy

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Identification of epileptogenic foci in patients with refractory epilepsy remains a significant diagnostic challenge. Magnetic resonance imaging studies frequently fail to reveal an anatomic origin for the seizures, and scalp electroencephalography is often limited to identification of the involved hemisphere. Functional imaging modalities such as PET and SPECT are more promising tools for this application because they reflect the functional pathology associated with the seizure. These changes are more pronounced ictally, but until recently, no radiopharmaceutical was available that could be used routinely for ictal SPECT. The present study was therefore undertaken to determine whether ^{99m}Tc-bicisate could be used in ictal SPECT in pediatric patients with refractory epilepsy, to compare the patterns of ictal and interictal blood flow in these patients and to compare the localization information provided by ictal SPECT with that available from other techniques. **Methods:** Technetium-99m-bicisate/SPECT was compared prospectively with scalp EEG for its ability to identify a possible seizure focus in pediatric patients with refractory epilepsy. Ictal and interictal SPECT studies were performed in 10 patients (3–19 yr old, mean age 10.9 ± 4.3 yr; 7 female, 3 male) in whom MRI scans revealed no lesions that might be responsible for the seizures. **Results:** Ictal SPECT was performed in all patients, and all ictal studies revealed focal perfusion abnormalities. By comparison, four of the interictal SPECT studies showed regional hypoperfusion that corresponded to the regions of hyperperfusion in the ictal studies, and three showed regional hyperperfusion corresponding to the hyperperfused regions in the ictal studies. Three interictal studies revealed no abnormal perfusion. Scalp EEG provided localization information in five patients. **Conclusion:** These initial results suggest that ictal SPECT with ^{99m}Tc-bicisate is a more promising tool for the identification of epileptogenic foci than interictal SPECT or scalp EEG in patients without focal abnormalities on MRI.

Key Words: technetium-99m-bicisate; epilepsy; SPECT; pediatrics

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Surgical ablation of the epileptogenic focus in patients with refractory seizures results in nearly complete elimination of the seizures in more than 75% of patients (*1,2*). More than 50,000 people in the United States alone could benefit from this surgical procedure (*3,4*). Unfortunately, localization of the seizure focus is frequently difficult. Only about 500 patients each year actually undergo surgery, in large part because of the problems associated with precisely localizing the seizure focus (*4*). The development of a relatively noninvasive method that provides precise localization of the seizure focus may allow more patients to benefit from surgery.

The most common method of focus localization is scalp electroencephalography (EEG), but the information provided by EEG is often limited to the identification of the involved hemisphere rather than the actual focus (*4–6*). More precise localization information can be obtained with depth electrodes or cortical grids, but both of these methods involve significant surgical risk and expense (*7*).

Because seizures are accompanied by changes in regional cerebral blood flow (rCBF) and metabolism, radiopharmaceuticals that reflect rCBF or metabolism can be used to identify the seizure focus (*8*). The metabolic changes associated with the seizure focus can be imaged using the ^{18}F-labeled glucose analog fluorodeoxyglucose ([^{18}F]FDG) and PET in about 75% of patients (*8–10*). At some centers, the localization information provided by [^{18}F]FDG PET has allowed decisions about surgical excision of seizure foci to be made without the need for coriticography (*6,10–14*). The sensitivity of PET might be even higher if ictal studies could be obtained because the metabolic changes are more localized ictally than interictally (*15–17*). Images obtained with [^{18}F]FDG, however, reflect a time-weighted average of glucose utilization over the 30–40-min uptake time of the tracer, which is much longer than the typical seizure duration of only several minutes (*8,18,19*). This disadvantage might be offset by administration of the tracer at seizure onset, but the relatively short half-life of ^{18}F (110 min) makes this difficult to accomplish on a routine basis (*8*). Additional limitations of [^{18}F]FDG PET include the high cost and limited availability.

SPECT is more widely available than PET and has been used to obtain ictal perfusion studies to identify seizure foci (*15–17,20*). The radiopharmaceutical that has been used in most of these studies, however, ^{99m}Tc-HMPAO has a shelf life of only 30 min, making it extremely difficult to use for ictal studies because it must be reconstituted at the time of the seizure (*15–17*), and the normal preparation time is longer than the typical seizure (<2 min). Therefore, unless unusual steps are taken to shorten the preparation time, the patient will be injected postictally rather then ictally. A more practical approach is to use a radiopharmaceutical with a longer shelf life.

The rCBF agent ^{99m}Tc-bisicate has a shelf life of more than 6 hr after reconstitution (*21*), making it more suitable for obtaining ictal SPECT studies, but it has only recently become available in the United States. The evaluation of ictal rCBF with this agent requires only that a precalibrated dose be available at the patient's bedside so that it can be administered at the onset of the seizure. The feasibility of this technique was demonstrated in a recent study by Grunwald et al. (*20*) of the use of ^{99m}Tc-bicisate SPECT in primarily adult patients with refractory epilepsy. However, that study included only one pediatric patient and did not exclude patients with focal MRI abnormalities such as tumors.

In patients with epilepsy with focal anatomic abnormalities identified by MRI, the question of seizure focus identification is one of confirmation that the lesion is in fact the seizure focus. In these patients, ictal SPECT may provide this confirmation and allow surgical excision of the lesion without the need for

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invasive EEG. In patients without focal MRI-identified lesions, the ultimate objective is to determine whether ictal SPECT or combined interictal/ictal SPECT can provide adequate identification of the seizure focus so that the patient can proceed to surgery without the need for electrocorticography. An intermediate objective would be to use the ictal SPECT results to guide electrocorticography and thereby minimize the associated risks and maximize the possibility that the seizure focus will be located.

As a first step toward these broader objectives, the present study was undertaken to (a) determine whether ^{99m}Tc-bicisate facilitated ictal SPECT in children with refractory epilepsy; (b) compare ictal and interictal rCBF in these patients; and (c) compare the localization information provided by ^{99m}Tc-bicisate SPECT with that provided by EEG in patients without MRI-identified structural lesions.

MATERIALS AND METHODS

Patients

The protocol was approved by the Children's Hospital Clinical Investigation Committee, and informed consent was obtained from each patient or their guardian before enrollment of the patient in the study. All patients admitted to the Children's Hospital Neuroscience Unit for presurgical evaluation of refractory epilepsy who had no MRI evidence of focal anatomic abnormalities were candidates for admission to this protocol. While in the neuroscience unit, patients were continuously monitored (EEG, video), and all seizures were noted. Paired ictal and interictal studies were obtained in 10 patients (3–19 yr old, mean age 10.9 ± 4.3 yr; 7 female, 3 male). Ictal studies were obtained in all patients with ^{99m}Tc-bicisate, and a ^{99m}Tc-HMPAO ictal study was obtained in one patient serendipitously. Three interictal studies were obtained with ^{99m}Tc-HMPAO before enrollment of the patients in the ^{99m}Tc-bicisate protocol. Because the primary concern of the present study was evaluation of ^{99m}Tc-bicisate for ictal studies, the interictal studies for these patients were not repeated with ^{99m}Tc-bicisate. The remaining seven interictal studies were obtained with ^{99m}Tc-bicisate.

MRI

The MR images were recorded with proton-density (TR 2000 ms/TE 17 ms) and T2 (TR 3200 ms/TE 85 ms) fast spin-echo sequences using a 1.5-T device (Signa; GE Corp., Milwaukee, WI). Typically, studies consisted of 18 slices of 256 × 256 pixels with a slice thickness of 3–5 mm, gaps of 0–3 mm and 0.94-mm × 0.94-mm pixels.

Radiopharmaceutical

Technetium-99m-bicisate was used under a physician-sponsored investigational new drug (IND) protocol. Each patient received 0.3 mCi (11 MBq)/kg ^{99m}Tc-bicisate (minimum dose 5 mCi [185 MBq], maximum dose 20 mCi [740 MBq]).

Ictal Studies

For ictal studies, an intravenous line was established and maintained, and a shielded syringe containing the ^{99m}Tc-bicisate was kept at the patient's bedside while the patient was monitored. A calibration table was prepared of administered dose (in milliliters) versus time, including an expiration time 6 hr after reconstitution of the kit. A single dose was prepared for each patient each day that they remained in the epilepsy unit. A selected group of the neuroscience nursing staff who were responsible for monitoring the patients were trained in basic radiation safety, specifically for the administration of ^{99m}Tc-bicisate under this protocol. When a seizure was noted by either the EEG or nursing staff, with subsequent EEG confirmation, the agent was administered by the attending nurse as quickly as possible after seizure onset, typically within 5–10 sec and no later than 30 sec after seizure onset.

Interictal Studies

Interictal studies were frequently obtained by injection of the ^{99m}Tc-bicisate that was prepared for an ictal study but was nearing its expiration time because the patient was seizure free during this 5–6-hr period. In the remaining cases, the patient was seizure free for at least 1–2 hr before injection.

Brain SPECT

Brain SPECT was performed in the Division of Nuclear Medicine 1–4 hr after administration of the tracer using a Siemens MultiSpect-3 system equipped with high- or ultrahigh-resolution collimators (Siemens Gammasonics, Hoffman Estates, IL). The FWHM resolution (in air) of this system is 7.5 mm, and it is capable of resolving objects as small as 5 mm in diameter. The rotation radius was 12.5 cm. Data were recorded for 120 steps of 30 sec each, with 3 degrees per step around the patient's head. Images were reconstructed by filtered backprojection using a Butterworth filter, and a Chang attenuation correction was applied. A 128 × 128 × 128-pixel image matrix was used for both data acquisition and display with a 2.46-mm slice thickness.

Image Analysis

The ictal and interictal studies were aligned along the orbitomeatal axis, normalized and coregistered using a program developed at Children's Hospital. The images were then evaluated independently by at least two nuclear medicine physicians (PJR, LOT, STT) experienced in the interpretation of cerebral perfusion SPECT. The same color table was used by all observers. Initial interpretations were performed independently, in random order, by observers blinded to the patient's clinical history and to the interpretations of the other observers. In cases of disagreement between observers, a consensus approach was used. Image assessment was qualitative, with observers noting areas of asymmetry in each image. After the initial assessment, the ictal and interictal studies were paired, and qualitative observations were made about the differences between the ictal and interictal images.

RESULTS

Non-SPECT data for the patients in the present study are summarized in Table 1, and the SPECT and EEG results are compared in Table 2. No adverse reactions attributable to administration of ^{99m}Tc-bicisate were observed in any of the patients. When the different localizing modalities are compared for their ability to identify a focus, it is important to note that patients whose MRI examinations revealed focal lesions were excluded from the protocol. Surface EEG was considered localizing if it revealed both the hemisphere and lobe or lobes of the seizure focus. Using these criteria, EEG was localizing in five patients (Patients 5, 6, 7, 8 and 10). Addition of the intracranial EEG data (when available) provided localizing information for one additional patient (Patient 1), leaving four patients in whom a focus was not clearly identified (Patients 2, 3, 4 and 9).

Interictal SPECT

Interictal SPECT revealed perfusion abnormalities in 7 of 10 patients (generally decreased rCBF in the involved lobe or hemisphere). The abnormalities included hypoperfusion in four patients and hyperperfusion in three. All the hypoperfused regions involved the temporal lobe. These same regions were hyperperfused in the ictal study. Two patients also had hypoperfusion of the frontal (Patient 1) and parieto-occipital regions (Patient 10). In the three patients with interictal hyperperfusion, the regions corresponded to the hyperperfused regions in the

TABLE 1
Non-SPECT Focus Localization

Patient no.	Sex	Age (yr)	History	Surface EEG	Grids	Corticography	Seizure focus (w/o SPECT)
1	F	11	CP, RH, onset at 9 mo	Interictal: broadly distributed R-sided spikes, sharp waves Ictal: generalized discharges followed by R-sided discharges	Ictal: R anteromesio-temporal lobe discharges	R anteromesial discharges	R anteromesiotemporal
2	F	3	CP, 2°GTC, onset at 8 mo	Interictal: normal Ictal: unclear; possible bilateral temporal lobe onset; L > R	Not done	Not done	L temporal
3	F	9	CP, 2°GTC, RH, onset at 3 d, R upper extremities	Interictal: bilateral centrotemporal spikes Ictal: no clear focal onset, electrodecremental followed by generalized slowing	Not done	Not done	Possibly frontal onset
4	F	12	SP, 2°GTC, RH, onset at 11 yr, throat, L face, arm	Interictal: R central spikes Ictal: R hemispheric discharges	Same as surface EEG	Same as surface EEG	R hemisphere (Rasmussen's?)
5	F	14	GTC, RH, onset at 12 yr, R hand, arm, face	Interictal: L central spikes, L slowing Ictal: L central spikes and spike–wave	Not done	Not done	L central (Rasmussen's?)
6	M	19	CP, RH, onset at 13 yr, staring, jaw twitching, incontinence	Interictal: L temporal slowing Ictal: L anterior temporal region	Not done	Not done	L temporal
7	M	10	CP, RH, onset at 5 yr, head movement	Interictal: L frontal Ictal: No clear abnormality	Not done	Not done	L frontal
8	F	10	CP, SP, 2°GTC, LH, onset at 3 wk, R eye deviation, R arm/leg twitching	Interictal: L central and midline spikes, slowing on L Ictal: L central and midline spikes	Same as surface EEG	Same as surface EEG	L mesial frontal
9	M	14	CP, 2°GTC, RH, onset at 4 yr, absence, head drop	Interictal: generalized spike–wave Ictal: generalized spike–wave	Bifrontal spike–wave	Bifrontal spike–wave	Possibly R frontal
10	F	7	SP, CP, RH, onset at 2 yr, R facial, R arm twitching	Interictal: R frontal slowing Ictal: R frontal slow activity	Not localizing	Not localizing	R frontal

CP = complex partial; RH = right handed; R = right; 2°GTC = secondarily generalized tonic–clonic; EEG = electroencephalography; L = left; SP = simple partial; LH = left handed.

ictal studies, except that the hyperperfusion was more pronounced in the ictal study. In general, the perfusion changes were less well defined in the interictal than the ictal studies.

Ictal SPECT

Ictal SPECT results were interpreted as abnormal in all 10 patients. Focal hyperperfusion was observed most commonly in the temporal (10 patients) and parietal lobes (7 patients). Two patients also had hyperperfusion of the putamen, and one had fronto-occipital hyperperfusion. Hyperperfused regions corresponded to the regions of abnormal perfusion observed on interictal SPECT in all patients. However, ictal SPECT sometimes revealed additional areas of abnormal perfusion not seen in the interictal study (e.g., Patients 1 and 4). There were also distinct areas of ictal hyperperfusion in the three patients in whom the interictal study results were considered normal.

Only two patients (Patients 4 and 7) had studies consistent with the classic perfusion pattern of complex partial epilepsy—ictal hyperperfusion and interictal hypoperfusion. In Patient 4, surface EEG suggested right central seizure onset, as did cortical grids and corticography. Interictal SPECT in this patient showed slight right temporal hypoperfusion, and ictal SPECT showed right temporal hyperperfusion as well as hyperperfusion of the right basal ganglia. In Patient 7, EEG suggested a left frontal lobe seizure focus, whereas ictal and interictal SPECT suggested right mesiotemporal focus.

Example 1 (Patient 3)

Patient 3 was a 9-yr-old, mildly retarded, right-handed girl with complex partial seizures, including secondary generalization (Fig. 1). The seizures involved predominantly clonic movements of the right upper extremity. The ictal EEG was

TABLE 2
Comparison of SPECT and Non-SPECT Focus Localization Information

Patient no.	Interictal SPECT (agent)	Ictal SPECT	MRI	EEG
1	R frontotemporal, hypo (^{99m}Tc-bicisate)	R upper frontal cortex, hyper; R frontotemporal, hypo	Nonlocalizing	R anteromesiotemporal
2	Normal (^{99m}Tc-HMPAO)	L prefrontal, L parietotemporal, L occipitotemporal, hyper; L perisylvian, hypo	Slightly delayed myelination	L temporal
3	Normal (^{99m}Tc-bicisate)	L caudate nucleus, L temporal, hyper; L cortex, hypo	Nonlocalizing	Possibly frontal onset
4	Slight R temporal, hypo (^{99m}Tc-bicisate)	R basal ganglia, R temporal, hyper	R sulci, fissures more prominent	R hemisphere
5	Normal (^{99m}Tc-HMPAO)	R basal ganglia, posteromesial aspect of R temporal, hyper	Nonlocalizing	L central
6	L mesiotemporal, slight hyper (^{99m}Tc-bicisate)	L mesiotemporal–caudate, hyper	Nonlocalizing	L temporal
7	R mesiotemporal, hypo (^{99m}Tc-bicisate)	R mesiotemporal, hyper	Nonlocalizing	L frontal
8	R frontotemporal, R basal ganglia, slight hyper (^{99m}Tc-bicisate)	R frontotemporal, R basal ganglia, hyper (greater than interictal)	Nonlocalizing	L mesial frontal
9	Multiple foci in R frontal, basal ganglia, mesiotemporal regions, hyper (^{99m}Tc-bicisate)	Multiple foci in R frontal, basal ganglia, mesiotemporal regions, hyper (greater than interictal)	Nonlocalizing	Possibly R frontal
10	R temporoparietal, L parieto-occipital, slight hypo (^{99m}Tc-HMPAO)	R posterior frontotemporal, hyper	Nonlocalizing	R frontal

EEG = electroencephalography; R = right; hypo = hypoperfusion; hyper = hyperperfusion; L = left.

electrodecremental, followed by generalized slowing with no clear focal onset, and the interictal EEG showed bilateral centrotemporal spikes. The MRI was nonlocalizing.

Interictal SPECT results were considered normal. Ictal SPECT showed increased tracer uptake in the left caudate nucleus and in left temporal lobe. Decreased tracer uptake was seen in the cortical regions of the left hemisphere.

Example 2 (Patient 10)

Patient 2 was a 7-yr-old girl with a history of seizures beginning at age 2 that included the right side of the face and the right arm and left arm posturing (Fig. 2). These became more frequent and severe at the age of 6 and included breath holding and screaming. An MRI of the head was nonlocalizing. The EEG suggested increased activity on the right, but no seizure focus was identified. Intracranial EEG identified a left frontal focus.

The interictal SPECT showed slight hypoperfusion of the right temporoparietal and left parieto-occipital regions. Ictal SPECT with ^{99m}Tc-HMPAO was obtained serendipitously and revealed focal hyperperfusion in the right posterior frontotemporal region. Ictal SPECT with ^{99m}Tc-bicisate also showed focal hyperperfusion in the right posterior frontotemporal region but with the hyperperfused regions more sharply defined than with ^{99m}Tc-HMPAO.

DISCUSSION

For patients with medically refractory seizures, the diagnostic objective is to identify as precisely as possible the seizure focus. If surgery is contemplated, it is important that the excised region be as small as possible. This precision cannot be achieved with scalp EEG because the regions identified are typically relatively large. More invasive EEG methods, such as cortical grids and depth electrodes, provide greater preci sion than scalp EEG but with the limitation of significant surgical risk (*7*).

Interictal [^{18}F]FDG PET has replaced cortical grids and depth electrodes at some centers because it is believed to be as least as precise as corticography and less invasive (*6,10–14*). However, this technology is still not widely available and, where available, is relatively expensive. Even if [^{18}F]FDG PET were to become more widely available, there still remains the practical limitation of trying to obtain an image that reflects glucose metabolism during a seizure that lasts only a few minutes with a tracer whose distribution reflects glucose utilization over a significantly longer period of time (*8,18,19*). This is a different situation from that encountered with either a SPECT or PET perfusion tracer, where the distribution of the tracer reflects blood flow at the time of injection. PET perfusion tracers are, however, not well suited for ictal epilepsy studies because of their very short half-lives.

In contrast to PET, SPECT is more widely available and less expensive, and the half-life of ^{99m}Tc is better suited to performing an ictal injection than that of PET radionuclides. Also, a perfusion tracer such as ^{99m}Tc-bicisate or ^{99m}Tc-HMPAO captures a snapshot of the blood flow at the time of injection rather than a time-weighted average over a time frame extending past the end of the seizure. Like PET, SPECT is minimally invasive and is capable of providing high-resolution (7–9 mm) three-dimensional rCBF information when carefully performed. However, to achieve maximum sensitivity, it is necessary to inject the tracer as soon as possible after seizure onset. Until recently, this was not routinely possible with ^{99m}Tc-HMPAO

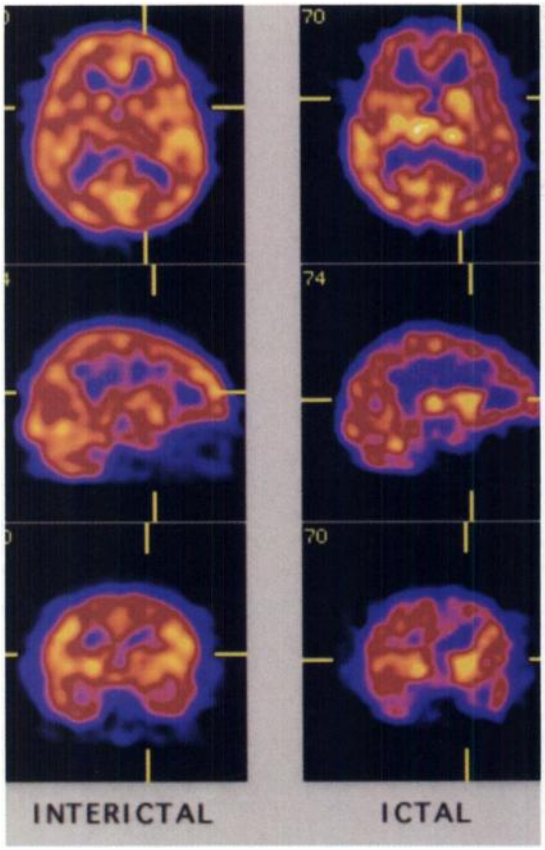

FIGURE 1. Patient 3. Interictal study results are normal, and ictal study shows increased tracer uptake in the left caudate nucleus and left temporal lobe. Decreased tracer uptake is seen in the cortical regions of the left hemisphere. C = coronal; R = right; S = saggital; T = transverse.

because its shelf life after reconstitution was only 30 min. After completion of this study, however, a more stable (4 hr) formulation of ^{99m}Tc-HMPAO became available. This is a significant improvement over the original kit, but the 6-hr shelf-life of ^{99m}Tc-bicisate still provides a 50% longer time window in which to capture the ictal event.

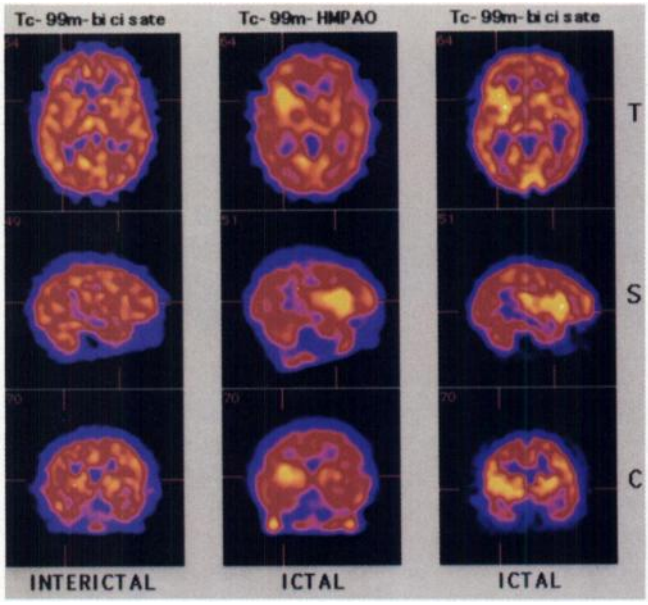

FIGURE 2. Patient 10. Interictal study shows slight hypoperfusion of the right temporoparietal and left parieto-occipital regions. Ictal studies show hyperperfusion of the posterofrontotemporal region with the hyperperfused regions more clearly defined in the ^{99m}Tc-bicisate study. C = coronal; R = right; S = sagittal; T = transverse.

Technetium-99m-bicisate is still more chemically stable than ^{99m}Tc-HMPAO, with a 2-hr shelf life. This greater chemical stability facilitates true ictal injections because the tracer can be at the patient's bedside for a longer period. Additional advantages of ^{99m}Tc-bicisate relative to ^{99m}Tc-HMPAO include slightly higher uptake in the brain, faster blood clearance, lower uptake in tissues surrounding the brain and lower whole-body radiation dose (*21,22*).

Because of the longer shelf life of ^{99m}Tc-bicisate, the chemical properties of the radiopharmaceutical are no longer the limiting factor to our ability to obtain ictal studies. Ictal studies were obtained in nearly every patient enrolled in the protocol who experienced a seizure while being monitored in the epilepsy unit. This is a significant improvement over the special tracer preparation procedures that were necessary to obtain ictal studies with ^{99m}Tc-HMPAO (*15–17*). The advantage of being able to obtain ictal studies can be seen in Table 1. Ictal SPECT revealed a region of hyperperfusion in every patient, whereas interictal SPECT revealed a perfusion abnormality in only 70%. Both of these results are similar to those of previous ictal and interictal SPECT studies obtained with ^{99m}Tc-HMPAO (*15–17,23*) and ^{99m}Tc-bicisate (*20*), but the ictal studies were easier to obtain with ^{99m}Tc-bicisate. In those cases where there were corresponding regions of ictal and interictal perfusion abnormalities, the regions of hyperperfusion in the ictal studies were generally smaller than those of hypoperfusion or hyperperfusion in the interictal studies. If the regions of ictal hyperperfusion are subsequently confirmed as seizure foci, it might be possible to eliminate seizures by excision of a smaller region of the brain than has previously been possible.

Confirmation that the hyperperfused foci identified by ictal ^{99m}Tc-bicisate SPECT correspond to the epileptogenic focus will only be available if excision of the identified region eliminates the seizures (*8*). To date, however, only one of these patients has had surgery. This patient (Patient 1) underwent a right temporal lobectomy that produced only partial relief from her seizures. The region identified as hypoperfused on both ictal and interictal SPECT and as electrically active by intracranial EEG was excised, but the frontal region that was identified as hyperperfused in the ictal SPECT was spared. This region might be responsible for the continued seizures.

CONCLUSION

As more experience with ictal ^{99m}Tc-bicisate SPECT is accumulated, it is anticipated that SPECT will assume a more prominent role in the preoperative decisions regarding localization of seizure foci, particularly for those patients in whom MRI fails to identify an anatomic abnormality. The more general availability of SPECT/MRI image registration software might also assist neurosurgeons in selecting smaller regions for excision. In the long-term, this may also allow more patients to benefit from surgery.

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Evaluation of Technetium-99m-ECD in Childhood Epilepsy

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In childhood epilepsy, it is difficult, but of critical importance, to determine whether surgical intervention might be beneficial for an individual patient. Because both established procedures—MRI and electroencephalography (EEG)—have limitations, interictal and ictal regional cerebral blood flow (rCBF) SPECT has proven to be a valuable adjunctive method in the presurgical evaluation of children. **Methods:** We evaluated the usefulness of the new rCBF tracer ^{99m}Tc-ECD in 14 children with focal epilepsy (mean age 9.7 yr). Eleven interictal and 8 ictal studies were performed. Results were correlated with ictal and interictal surface EEG, MRI and histological findings and the postsurgical outcome. **Results:** On the basis of the presurgical evaluation, nine patients underwent surgery. MRI studies demonstrated pathological features with possible relation to epilepsy in 50%. Overall, interictal ^{99m}Tc-ECD SPECT showed areas of hypoperfusion in 80% of patients. Ictal rCBF SPECT was informative in all patients, including one who showed bifrontal hyperperfusion in accordance with EEG results. **Conclusion:** Technetium-99m-ECD has proven to be of value for interictal and ictal rCBF SPECT in childhood epilepsy. No side effects during or after tracer administration were noticed. Ictal and interictal rCBF SPECT showed good correlation with MRI and EEG results in patients in whom correlation with the postoperative situation was possible and presented additional significant information in those patients with normal MRI and uninterpretable EEG results. No false lateralizations occurred. In children with focal epilepsy, interictal rCBF SPECT may accelerate the application of long-term electrocorticography (ECoG) in patients with normal MRI results. Ictal rCBF SPECT may also help to avoid ECoG, if a focal hyperperfusion correlates with a focal MRI abnormality, and the surface EEG gives no contradictory information.

Key Words: technetium-99m-ECD; SPECT; epilepsy; children

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Epilepsy is a common disease during childhood (*1*). Compared with epilepsy in adolescence, the variety of underlying reasons and their clinical appearance are much wider. The presurgical evaluation of many of these patients appears to be especially difficult because focal epilepsy is frequently associated with unclear symptomatology, and correlation of surface electroencephalographic (EEG) findings with regional pathology in epilepsy is difficult. Furthermore, in patients with multifocal epilepsy (e.g., Lennox-Gastaut syndrome [LGS]) (*2*), it is often difficult to identify the leading focus on the surface EEG, and MRI results are often normal in children.

In many patients with childhood epilepsy, a good prognosis can be expected. However, those children with partial seizures, especially those with multifocal epilepsy (e.g., LGS) (*3*), often have a poor prognosis for social and intellectual development because they are frequently refractory to medical treatment.

Some patients may benefit from epilepsy surgery. However, depiction of a subgroup that might benefit from surgery is more difficult in children than in adults. Although it seems logical to treat appropriate patients surgically as early as possible to allow their optimal development, it is also clinically necessary to allow some delay between the onset of an epileptic seizure and the decision to perform surgery in some cases. This is because effective and accepted investigational procedures for detection of epileptogenic foci or associated morphological abnormalities may need time to become clearly evident. For example, ictal EEG may not be able to lateralize or, if so, to provide appropriate spatial resolution if the generalization of a seizure is too fast to identify the possible origin. On this basis, it might be difficult even to distinguish between primary or secondary generalization because interictal EEG abnormalities may also be generalized or widely abandoned. Furthermore, seizure symptomatology is sometimes unclassifiable, and