Drugs-resistant epilepsy is a serious medical problem, associated with neuropsychiatric and neuropsychological comorbidities, social and economic disability, diminished quality of life, and increased mortality compared to the general population. Surgery may be beneficial in carefully selected patients. Postoperative seizures depend on accurate localization of epileptogenic zones. Comprehensive neuropsychological evaluation and appropriate imaging studies must be performed as well to assess the risks of resection.

Positron emission tomography (PET) using [18F]-fluoro-deoxyglucose (FDG) and single-photon emission computed tomography (SPECT) using either 99mTc-ethyl cysteinate dimer (ECD) or 99mTc-hexamethyl propylene amine oxime (HMPAO) are now standard procedures for preoperative evaluation of patients with epilepsy.

PET cameras generally have somewhat better resolution than SPECT, although recent advances have reduced the difference. Both modalities suffer from the risk of “partial volume effects” due to which the camera may not be able to resolve small lesions, or be affected by the volume loss that can occur in lesions such as mesial temporal sclerosis (MTS). Magnetic resonance imaging (MRI)–based partial volume correction routines can obviate much of this problem, and the advent of combined scanners, for example PET/MR, should improve coregistration of structural and functional images.

Advances in MRI, may reduce the importance of PET and SPECT for preoperative evaluation. Functional MRI, for example, has ended the temporary use of [15O]H2O PET for presurgical functional mapping. However, PET and SPECT have been used to investigate epilepsy comorbidities, particularly psychiatric disorders, and pathophysiology, through neurotransmitter receptor binding (the latter approach has been used (less frequently) to support focus localization as well). These applications should become increasingly valuable with the development of new ligands that can image important systems such as excitatory amino acids and immunomodulation. PET’s role in particular in helping to elucidate the pathophysiology of epilepsy may become more important than its clinical value for seizure focus localization.

FDG-PET Seizure Focus Localization

About 80% of patients with temporal lobe epileptic foci have hypometabolism on [18F]FDG-PET scans. Some more recent studies have found that up to 100% of patients have hypometabolism. Others found only 60%-70% positive PET scans. The difference depends in part on analytic technique, but the proportion of patients with abnormal MRI probably is more important.

In a meta-analysis of 46 studies from 1992-2006, study design heterogeneity made overall assessment difficult. PET hypometabolism alone was thought to have a predictive value of 80% for “good” outcome (not always equivalent to being seizure-free) in patients with normal MRI, and 72% in patients with nonlocalized ictal scalp electroencephalographic (EEG) discharges, but not to improve accuracy for seizure focus localization or surgery outcome in patients with congruent ictal scalp EEG and MRI localization.

In a study of [18F]FDG-PET in 194 adults including 64 with temporal lobe epilepsy (TLE), 66 with front lobe epilepsy (FLE), 38 with seizure foci in other extratemporal regions, and...
26 with a focus including temporal lobe and additional regions, 158 had normal MRI. PET scans were normal in 37%, showed unilateral hypometabolism in 50.5% (67% in TLE vs 52% in FLE) and bilateral hypometabolism in 12% of patients. PET was thought to provide useful information in 53%, leading directly to surgery in only 6%, but helping in planning intracranial EEG 35%. Patients with focal hypometabolism were five times more likely to be selected for surgery than those without hypometabolism.

Several studies have shown that patients with normal MRI but anterior temporal hypometabolism are good surgical candidates (Fig. 1). Two large series showed similar results. Of 193 patients, 46 had negative MRI but positive PET; there was no difference in surgical outcome. Overall, 79% of MRI-negative PET-positive TLE patients were seizure-free 2 years after surgery, compared to 82% of with MTS on MRI as well as hypometabolism. In a recent study, FDG-PET performed better than either MRI diffusion tensor imaging or cortical thickness measurement for identifying temporal lobe foci. The authors used a stepwise logistic regression model that showed the two MRI modalities combined did not add localizing value to [18F]FDG-PET alone. Bitemporal hypometabolism is associated with less-well localized ictal epileptiform onsets and may be a negative surgical prognostic indicator.

For FLE patients who showed good outcome after surgical resection, 73% of patients with, and 36% without MRI structural lesions had focal hypometabolism. Patients with extratemporal seizure foci were more likely to be seizure-free if there was no hypometabolism either contralateral to the lesion, or if ipsilateral, in a different lobe. Hypometabolism that is not contiguous with, or distant from the seizure focus, as opposed to perifocal hypometabolism, may be a negative prognostic factor in patients with both mesial temporal and neocortical electrographic seizure onsets.

At present there is little evidence to suggest that quantitative approaches such as statistical parametric mapping are more accurate for localization of seizure foci than “expert” visual analysis. However, it is important for neurologists treating patients with epilepsy to review [18F]FDG-PET (as well as MRI) images themselves, as they are able to make important clinical and electrographic correlations with the imaging data. For example, re-examination of MRI images in patients with hypometabolism and “normal” MRI, particularly with neocortical or extratemporal or foci, may show initially undetected subtle lesions such as focal cortical dysplasia (FCD). Some investigators suggest that when temporal hypometabolism extends beyond the limits of an MRI lesion such as MTS, wider resection may improve outcome. However, in another study, the volume of [18F]FDG- as well as [11C-FMZ PET abnormality resected were not significantly related to outcome.

The correlation between the degree of mesial temporal neuronal loss and hypometabolism is inexact, and hypometabolism extends beyond the epileptogenic zone defined by pathology and electrophysiology to include, in mesial TLE, ipsilateral frontal cortex, thalamus, and insula. The physiologic basis for hypometabolism in the absence of MRI lesions is uncertain, but may be related to decreased synaptic activity, impaired maintenance of membrane potentials, differences in hippocampal surface anatomy, or alterations in adjacent white matter tracts on diffusion tensor imaging.

The extent of epileptic networks determined by seizure spread on ictal EEG recordings correlated strongly with patterns of hypometabolism in 114 patients with mesial TLE. Data from studies of FCD suggest that hypometabolism is associated with reduced mitochondrial complex IV function, but not the extent of the structural abnormality. However, there was no difference in mean hippocampal hilar neuron and dentate h...
gyrus granule cell densities between patients who all had focal hypometabolism, but with and without observable MRI evidence of MTS.\textsuperscript{13}

The clinical role of FDG-PET in nonfocal epilepsy syndromes is less certain.

Children with infantile spasms and normal structural MRI have hypometabolism in parieto-temporo-occipital cortex, associated with “occult” malformations of cortical development; FDG-PET imaging may help guide resection strategy.\textsuperscript{35}

**Clinical Applications of Other PET Ligands**

Several other PET ligands, particularly [11C]Flumazenil (FMZ) may have localizing potential for patients with focal epilepsy syndromes. Reduced benzodiazepine receptor binding on [11C]FMZ PET ipsilateral to temporal lobe foci occasionally may detect abnormal regions not seen on [18F]FDG-PET.\textsuperscript{36–39} In a study of 100 patients, about 98% had focal reduced GABA-benzodiazepine receptor binding, compared to about 90% with regional hypometabolism and 85% with abnormal MRI,\textsuperscript{40} suggesting that [11C]FMZ PET could detect focal abnormalities in a very high proportion of MRI-negative focal epilepsy patients. In another study only about 40% of patients with normal MRI had reduced [11C]FMZ binding, a proportion similar to [18F]FDG-PET.\textsuperscript{41} [11C]FMZ PET at least partially detected seizure onset zones in 10 children with neocortical epilepsy, while [18F]FDG-PET showed congruent hypometabolism in only eight.\textsuperscript{42} Neither PET study was able to delineate regions of rapid seizure spread. FMZ PET was more sensitive than FDG-PET for detection of neocortical seizure onset in children with extra-TLE.\textsuperscript{43}

[18F]Flumazenil has been suggested as an alternative, and more practical ligand to [11C]FMZ due to its longer ligand half-life.\textsuperscript{44}

Some [11C]FMZ PET studies found binding increases and decreases in periventricular white matter in patients with both temporal and extratemporal foci and normal MRI that were presumed to identify periventricular nodular heterotopias.\textsuperscript{45,46} Detection of these regions of increased periventricular [11C]FMZ binding was associated with poor outcome after temporal lobectomy. In a subsequent study, 16 patients with MTS had [18F]FDG and [11C]FMZ PET. On a group level, non–seizure free vs SF patients had greater periventricular increases with both tracers, but individually FMZ-PET was more sensitive. Against controls, non–seizure free patients showed more prominent periventricular [11C]FMZ and [18F]FDG signal increases than SF patients. However FMZ had greater sensitivity for FDG and correlation with outcome.\textsuperscript{47}

[11C] α-methyl-l-tryptophan (AMT) may be able to differentiate epileptogenic from “silent” tubers in children with tuberous Sclerosis.\textsuperscript{48} Overall, 58% of patients with nonlocalized EEG had localized AMT-PET. In another study, only 2 of 12 patients showed clearly increased uptake; although sensitivity was low, specificity was 100%.\textsuperscript{49} Increased binding has been reported in patients with FCD, particularly type IIB, may have increased [11]C-AMT binding.\textsuperscript{50}

**Clinical Applications of SPECT Imaging**

Subtraction of interictal from ictal SPECT images, with coregistration to MRI, has been reported to predict outcome after both temporal and extratemporal epilepsy surgery.\textsuperscript{51,52} (Fig. 2). Injection as soon as possible (preferably within 15 seconds) after seizure onset is crucial for accurate localization. Combining “hyperperfusion” with “hypoperfusion” images may increase seizure focus detection. Overall, 63% of patients with TLE, and 58% with extratemporal lobe epilepsy (ETLE), have seizure-free surgical outcome if ictal SPECT cerebral blood flow (CBF) abnormalities are concordant with the resected region, but only 20% when concordance is absent.\textsuperscript{53}

In a study comparing ictal and interictal SPECT with EEG-IMRI, there were significant positive correlations between ictal hemodynamic changes and spikes in 96% of patients.\textsuperscript{54} Hyperperfusion was generally associated with ictal activity and hypoperfusion with interictal deactivation. SPECT CBF changes congruent with EEG discharges occurred in regions distant from presumed foci, such as cerebellum and basal ganglia.

Not all studies suggest ictal SPECT adds to preoperative evaluation; it has the added disadvantage of being an inpatient procedure. A comparison of 124 patients who had SPECT as part of their evaluation with 116 who did not showed no difference in the proportion offered surgery or invasive monitoring.\textsuperscript{55} Mean duration of hospital stay was longer, secondary generalized tonic-clonic seizure more frequent, and the cost of evaluation 35% higher for the SPECT group. No difference in surgical outcome was found. In children being evaluated for epilepsy surgery, mean length of hospital stay was 5.1 days when SPECT was performed, compared with 3.5 days when it was not.\textsuperscript{56}

Although 68% of patients with extratemporal epilepsy had localization on subtraction ictal SPECT coregistered to MRI (SISCOM), interictal and ictal EEG but not SPECT results were significant predictors of surgery outcome even when MRI was normal.\textsuperscript{57} A total of 58 patients, including both TLE and ETLE had structural magnetic resonance imaging (MRI), high-density electric source imaging (HD-ESI), and metabolic imaging (positron emission tomography [PET]; single-photon emission computed tomography [SPECT]); only MRI and HD-ESI significantly predicted seizure-free outcome after surgery.\textsuperscript{58}

Just as for [18F]FDG-PET, most studies suggest that the role of ictal SPECT when MRI shows hippocampal sclerosis is uncertain.\textsuperscript{59} One study found SPECT most valuable in confirming focus localization and helping to avoid invasive studies in patients with lesional mesial TLE but nonlocalizing ictal EEG or dual pathology but SPECT not in patients having either TLE or ETLE with normal MRI, since those patients needed depth or subdural investigation.\textsuperscript{60} Statistical parametric mapping–based analytic approaches increased the sensitivity of ictal-interictal SPECT from about 40%-70% for TLE, and 35%-55% for ETLE in patients with normal MRI.\textsuperscript{61}
There have been a series of comparisons between [18F]FDG-PET and ictal-interictal SPECT, usually showing comparable results for seizure focus localization and surgical outcome prediction. Combining modalities may improve results. A coregistration study found that combined PET, MRI, and SISCOM helped detect epileptogenic zones in 35 patients, particularly with normal MRI; SISCOM showed ictal hyperperfusion less frequently than PET hypometabolism. A total of 58 patients, including both TLE and ETLE had structural MRI, HD-ESI, and FDG-PET; single-photon emission computed tomography (SPECT); only MRI and HD-ESI significantly predicted seizure-free outcome after surgery.

When both FDG-PET and ictal SPECT were concordant with each other and with MRI and vEEG defined focus in a study of 123 patients, 62% were seizure-free at 5 years for extratemporal epilepsies, significantly more than if the studies were not concordant. However, for TLE, SPECT-PET concordance did not improve outcome. Several studies suggest that [18F]FDG-PET may be more sensitive for TLE, and SPECT for ETLE.

Fewer SPECT studies have been performed in patients with presumed nonfocal epilepsy syndromes than in patients being considered for surgery for focal epilepsy. In 10 patients with Lennox-Gastaut syndrome, isotope injections during tonic seizures and within 10 seconds of onset, found hyperperfusion in pons and cerebellar hemispheres and bilateral pericentral hypoperfusion. Later injection led to midline and lateral cerebellar hyperperfusion, and widespread bilateral frontal hypoperfusion. The findings suggested involvement of frontal attentional regions with pontine reticular formation.

Research Applications of PET Neurotransmitter Receptor Imaging

The serotonin (5HT)-1A receptor has been implicated in the pathophysiology of epilepsy as well as depression. 5HT1A receptor postsynaptic terminals are abundant in limbic regions, and their activation reduces glutamate release and hyperpolarizes hippocampal membranes. Several investigators found reduced binding in mesial temporal foci (Fig. 3). The reduction was present even after partial volume correction to account for volume loss in limbic structures such as hippocampus and amygdala. In combination with FDG-PET, 5HT1A receptor imaging may help predict outcome after temporal lobectomy.

In patients with depression, one of the most common epilepsy comorbidities, there was a significant relation between increasing scores on the Beck Depression inventory and the Montgomery-Asberg inventory and reduced 5HT1A receptor binding. Compared with healthy controls and patients who did not have a diagnosis of major depressive disorder on the structured clinical interview for DSM IV, depressed patients had lower 5HT1A binding. Since the structured clinical interview for DSM IV is designed to diagnose major depressive disorder even when overt symptoms, or an acute episode, are not present, the results suggest that patients with depression as...
well as epilepsy, have additive reductions of 5HT1A receptor binding as a trait-related phenomenon, persisting even when symptoms are not clinically evident. These results extend previous FDG-PET studies that showed ipsilateral or bifrontal hypometabolism in patients with both depression and epilepsy.73-77 Altered serotonergic neurotransmission forms a particularly strong link between epilepsy and depression. Reduced 5HT1A receptor binding had an effect on verbal memory scores (after correction for partial volume effects) that was additive to the influence of hippocampal atrophy, and independent of depression scales.78

PET studies using a ligand for the serotonin transporter activity was reduced in patients with both TLE and depression, as compared to subjects with TLE alone; both groups had reduced 5HT1A receptor binding.79 The transporter facilitates reuptake of serotonin into the presynaptic axon terminals after its release and interaction with postsynaptic receptors. It is possible that reduced transport, leading to reduced reuptake and thus increased synaptic 5HT availability, might represent a compensatory mechanism for 5HT1A receptor loss a clinical implication of the PET data is that selective serotonin reuptake blockers should be used in patients with epilepsy and comorbid depression.

Mu opiate-receptors were increased ipsilateral to epileptic foci in lateral, but not mesial, temporal structures; kappa receptors may be reduced.80-82 Increased H1 histamine and MAO-B binding potential, and decreased regional binding of [76Br]bromodexetemide, a muscarinic acetylcholine receptor antagonist, in the anterior hippocampus ipsilateral to epileptic foci could be explained by local glialis and neuronal loss.83-85 In patients with autosomal dominant nocturnal FLE, who have mutations in the nAChR alpha4 or beta2 subunit, PET using [18F]-F-A-85380, a high-affinity agonist at the alpha4beta2 nAChRs, showed increased binding in mesencephalon, pons, and cerebellum, and decreases in the dorsolateral prefrontal region when compared to control subjects.86 Several studies have shown alterations of dopamine receptor binding, with decreases in ipsilateral temporal lobe in TLE.87 Results varied depending on the ligand and analysis technique.88 Patients with MTS had reduced [18F]fallypride dopamine D2/D3 receptor binding potential significantly reduced in temporal lobe ipsilateral to seizure foci and bilateral putamen. There was a positive correlation between age at onset of epilepsy and [18F]FP BPDn in the ipsilateral temporal lobe and a negative correlation between epilepsy duration and [18F]FP BPDn in the temporal pole, suggesting progressive receptor loss with increasing length of seizure history.89 The N-methyl-D-aspartate (NMDA) receptor ligand [11C]-(S)-[N-methyl]ketamine, showed reduced tracer radioactivity in epilepticogenic temporal lobes, also possibly due to local atrophy.52 A recent study showed increased availability of the neurokinin-1 receptor in TLE, mirroring studies in experimental models that have suggest a role for substance P in epileptogenesis.91

Several variables, in addition to structural atrophy, might affect PET neuroreceptor imaging in epilepsy. The length of the seizure-free interval correlated with [11C]FMZ hippocampal binding; the shorter the interval, the lower bmax. In several cases, scans performed at different intervals after seizures show contradictory focus localization. Antiepileptic drugs (AEDs) or other agents affecting brain blood flow or metabolism, or receptor binding itself, might be important. Using [(18F)GE-179, a ligand that selectively binds to the open NMDA receptor ion channel, eight patients not taking antidepressants had globally increased binding compared to controls, while three taking antidepressants had decreased binding.93 No focal abnormalities clearly associated with MRI or EEG discharges were seen. These studies show the importance of controlled clinical conditions for interpretation of neurotransmitter receptor PET in epilepsy.

Several genetic epilepsy syndromes have been investigated using PET neuroreceptor imaging. Patients with ring chromosome 20 epilepsy have was decreased bilateral [18F]fluoro-L-DOPA uptake in putamen and caudate nucleus.94 Impaired dopamine uptake was reported in the midbrain of patients with juvenile myoclonic epilepsy.95 In patients with succinic semialdehyde dehydrogenase deficiency, an autosomal recessive disorder of GABA metabolism associated with cognitive impairment, ataxia, and seizures, PET using [11C]flumazenil detected reduced postsynaptic benzodiazepine receptor binding, probably due to down-regulation related to increased synaptic GABA levels.96

Research in PET Imaging of Inflammation in Epilepsy

Inflammation has been shown to play a role in a wide range of neuropsychiatric disorders, including epilepsy.97 [18F]FDG-PET may show focal increased metabolism in patients with anti-NMDA receptor encephalitis.98,99

Several PET ligands can be used to image the translocator protein 18 kDa (also known as the “peripheral benzodiazepine receptor”), a marker of activated microglia and reactive astrocytes. Studies using [11C]PK-11195 had shown increased binding in a patient with Rasmussen’s encephalitis.100 Several case reports have suggested potential value in localizing seizure foci. A 5-year old with intractable epilepsy and normal [18F]FDG-PET had an area of increased [11C]-PK-11195 binding co-localized with epileptiform discharges on EEG; resection led to seizure control and microglial activation was found on pathological examination.101 A patient with FCD had increased binding co-localized with EEG, MR, and [18F]FDG-PET seizure focus localization.102 Patients with TLE did not show increased binding in studies using [11C]PK-11195. However, with two newer ligands, [11C]PBR28 and 11C]DPA 714, increased brain uptake was present in a bilateral distribution compared with healthy volunteers, but significantly higher ipsilateral to the seizure focus in hippocampus, amygdala, and temporal neocortex in patients both with and without MTS, although the asymmetry was more pronounced in patients with hippocampal sclerosis than in those without (Fig. 4).103,104 Patients with FCD also had increased binding using these 2 new ligands. The results parallel studies in experimental epilepsy models including the kainic acid rat model.105 Using PK-11195, rats with spontaneous seizure after electrically kindled status epilepticus who
were responsive to phenobarbital, did not show greater binding than sham-control animals, while drug-resistant animals did.\textsuperscript{106} A possible link between inflammation and drug resistance is provided by P-glycoprotein (P-gP) transporters, which are upregulated in some patients with epilepsy. In a comparison of 14 pharmacoresistant patients, eight seizure-free patients, and 13 healthy controls, pharmacoresistant patients had higher P-glycoprotein activity than seizure-free patients in several temporal regions both ipsilateral and contralateral to seizure foci.\textsuperscript{107} Higher P-gp activity was associated with higher seizure frequency. Seven patients with drug-resistant TLE (R)-[11C]verapamil (VPM) PET before and after temporal lobectomy.\textsuperscript{108} Patients who became seizure-free off AEDs after surgery had higher preoperative ligand binding, and temporal lobe P-gP function before surgery, and reduced global P-gP function postoperatively, than those who did not become seizure-free off AEDs.

**SPECT Neuroreceptor Imaging**

SPECT has been used for neuroreceptor mapping studies much less frequently than PET, due to disadvantages in resolution and quantitation. The benzodiazepine receptor ligand [123I]-iomazenil was superior to interictal SPECT CBF studies for localizing seizure foci in TLE patients.\textsuperscript{109} In four patients with tuberous sclerosis complex, reduced [123I]-iomazenil binding was found in all tubers seen on MRI, but epileptogenic lesions were not distinguished.\textsuperscript{110} Seizure frequency was positively correlated with postsynaptic putamen and caudate D2 density measured with [123I]IBZM in ring chromosome 20 epilepsy patients; presynaptic transporter activity measured with [123I]ioflupane showed negative correlation with seizure activity.\textsuperscript{111} A SPECT ligand for translocator protein has not been used in epilepsy.

**PET and SPECT in Epilepsy Evaluation: Problems and Pitfalls**

Unfortunately the number of patients in most epilepsy nuclear imaging studies has been too small for definitive results. Prospective multicenter studies would have a much better chance of determining their optimal use, and preventing not only waste of resources but also unneeded radioactivity exposure. Clear guidelines have been developed that allow imaging studies to provide reasonably reliable evidence.\textsuperscript{112} These include clearly defining study populations and controls, prospective data collection, applying tests to all patients uniformly, data analysis blinded to patient identity and clinical characteristics, discussion of limitations and study power, and if surgical outcome is a study end point, objective assessment of postoperative seizure control.

FDG-PET is a more forgiving technique than ictal-interictal SPECT. However, interpretation may be made more difficult by seizures occurring during, or even immediately before tracer administration and the 30-40 minute uptake period. Unrecognized seizures may lead to false lateralization as hypermetabolism ipsilateral to the true seizure focus may make the contralateral cortex appear relatively hypometabolic. Recent seizure activity may produce altered patterns of metabolism on FDG-PET persisting for several days.\textsuperscript{113,114} Prior depth electrode implantation may cause hypometabolism.\textsuperscript{115} Large cortical malformations may have increased metabolism.\textsuperscript{116} Bilateral temporal hypometabolism may be more common on scans performed within 2 days of a seizure.\textsuperscript{117} If EEG monitoring cannot be performed, patients should be attended by an observer able to recognize seizure activity. Ictal SPECT requires constant video-EEG monitoring, as well as the ability to inject the tracer within 15-30 seconds after seizure onset. It is likely that neither technique adds much to concurrent MRI and EEG seizure focus localization.

The main pitfall in interpreting ictal-interictal SPECT studies is the effect of interval between seizure onset and injection. Longer intervals, depending on seizure type and duration, may lead to apparent ipsilateral hypometabolism, as well as more extensive CBF alterations associated with seizure spread. It is also crucial in planning epilepsy surgery to make sure that the seizure studied with SPECT is in fact a patient’s habitual event. If seizures are very short, it may be difficult to perform a true ictal injection. Hypermotor seizures may require measures to prevent patient injury that make injection difficult or impossible.
The choice of which study to use depends mainly on facilities and experience; imaging evaluation strategy for patients with epilepsy should be based on electroclinical classification. As long as patients are seizure-free on AEDs, there is no reason to perform clinical [18F]-FDG-PET or SPECT; there are only indicated when surgery is considered. Patients with clearly defined generalized, presumably genetic epilepsy syndromes such as childhood absence, juvenile absence or juvenile myoclonic epilepsy do not need imaging studies. For patients with presumed focal epilepsy syndromes, or those who do not have definite evidence of a genetic epilepsy syndrome, MRI is the first step. Identification of a seizure disorder depends on clinical and EEG data, and imaging, including PET and SPECT, should not be used as a diagnostic tool.

**PET and SPECT in Comprehensive Evaluation of Drug-Resistant Epilepsy**

Brain surgery has irrevocable effects, and should only be performed after careful discussion and consideration of all available data. PET and SPECT should be integrated into the overall patient evaluation (Fig. 5). Only limited data suggest that patients with focal MRI matching ictal EEG seizure focus localization and consistent clinical semiology may benefit from PET or SPECT. If MRI is normal, but PET or ictal SPECT clearly focal and consistent with clinical and EEG localization, surgery can be considered with or without invasive electrode studies (which may in any case be indicated for language and memory mapping. [11C]FMZ-PET may be considered as an additional potential localizing procedure. If MRI is multifocal, or discordant with EEG and clinical localization, PET, SPECT, or even both may be performed in an attempt to form a plan for invasive EEG evaluation. If these studies are unrevealing, the chance of finding a resectable focus may be very low, and other treatment options should be pursued.

**References**


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**Figure 5** Flow chart showing how PET and SPECT may contribute to evaluation of patients with drug-resistant epilepsy for possible surgery.
Presurgical focus localization in epilepsy


