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## Epilepsy

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# Epilepsy

**E**pilepsy is a common disorder, affecting approximately 0.5% to 1.0% of the United States population at any time with an incidence of 30.9 to 56.8 per 100,000.<sup>1</sup> It has been estimated that about 7%–8% of the population experiences at least 1 epileptic seizure during their lifetimes.<sup>2</sup> The basic mechanism of epileptic seizures has not been fully elucidated.

The classification of epileptic seizures by the International League Against Epilepsy was last revised in 1989 (Table 1).<sup>3</sup> The classification is important because etiologic diagnosis, appropriate treatment, and accurate prognostication all depend on the correct identification of seizures and epilepsy. There are 2 main seizure types: partial seizures and primary generalized seizures. Partial (formerly referred to as focal) seizures show either clinical or EEG evidence of onset from a localized area within the cerebral hemisphere. The nature of the signs and symptoms in most cases indicate the region of the brain involved by the epileptic process. Partial seizures are designated as simple or complex. Complex partial seizures are associated with loss of consciousness. In simple seizures, the epileptic process is usually confined to neocortical structures, and the limbic system and brain stem are spared. Most simple seizures are less disabling than those associated with loss of consciousness. Partial seizures can spread and develop into secondarily generalized seizures. Primary generalized seizures originate simultaneously from both cerebral hemispheres, and clinical manifestations involve both sides of the body. Primary generalized seizures first occur at an earlier age, and are more likely to be associated with a family history of seizure disorders, but are less likely to be associated with focal cerebral lesions. Some seizures remain unclassified because the underlying mechanism of their origin or propagation is unknown.<sup>2</sup>

Certain types of seizure disorders are likely to be associated with structural brain lesions, including tumors, infection, infarction, traumatic brain injury, vascular malformations, developmental abnormalities, and seizure-associated brain pathology,<sup>4</sup> whereas others are not. Hence, knowledge of seizure types helps to determine whether neuroimaging is clinically indicated and what type of study is appropriate (Table 2).

While the imaging evaluation of epilepsy was greatly advanced by the clinical introduction of CT in the early 1970s<sup>5,6</sup> because of its superior soft tissue contrast, multiplanar imaging capability, and lack of beam hardening artifacts, virtually all the substrates of epilepsy are visualized with greater sensitivity and accuracy by MR imaging.<sup>7–15</sup> As a result, MR imag-

**Table 1: Outline of the International Classification of Epileptic Seizures**

I. Partial Seizures (seizures with focal onset)
i) Simple partial seizures (consciousness not impaired)
1) With motor signs
2) With somatosensory or special-sensory symptoms
3) With autonomic symptoms or signs
4) With psychic symptoms (disturbance of higher cerebral functions)
ii) Complex partial seizures (consciousness impaired)
1) Starting as simple partial seizures
a) Without automatisms
b) With automatisms
c) With impairment of consciousness at onset without automatisms (impairment of consciousness only)
iii) Partial seizures evolving into secondarily generalized seizures
II. Generalized Seizures
i) Absence seizures and atypical absence seizures (may have the following components):
Mild clonic, atonic, tonic, or autonomic activities, or automatic behavior
ii) Myoclonic seizures
iii) Clonic seizures
iv) Tonic seizures
v) Tonic-clonic seizures
vi) Atonic seizures
III. Unclassified Epileptic Seizures

ing has become the technique of choice for high-resolution structural imaging in epilepsy. Although routine evaluation techniques of all clinically available scanner field strengths may be sufficient for determining mass lesions, optimized protocols for scans obtained on high-field (>1.5 T) scanners may be necessary for evaluating partial complex epilepsy, requiring scrutiny of the hippocampus and temporal lobe for atrophy and subtle signal intensity alteration, as well as for detecting certain structural abnormalities such as cortical dysplasias, hamartomas, and other developmental abnormalities.<sup>8,9,16–21</sup> Anatomic imaging identifies focal abnormality in up to 51% of patients with partial epilepsy.<sup>22</sup> With the widespread clinical availability of high-performance MR imaging systems, a comprehensive MR imaging examination, with functional techniques providing additional information, adding corroborative information, and improving overall accuracy, may in the future be of even greater value in epilepsy.

Although the data provided by MR imaging are essential in the presurgical evaluation of patients with medically refractory epilepsy, structurally detectable abnormalities are absent in many patients. In these patients, functional studies provide useful information on the location of the seizure focus. Functional imaging techniques, including positron emission tomography (PET), single-photon emission CT (SPECT), magnetic source imaging (MSI), and functional MR imaging

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**Table 2: Clinical condition: epilepsy**

	MRI head without contrast	MRI head without and with contrast	CT head without and with contrast	CT head without contrast	FDG-PET head	SPECT head	fMRI head	MEG/ MSI	MRA head
Chronic epilepsy, poor therapeutic response. Surgery candidate.	8	8	6	5	7 <sup>a</sup>	5 <sup>a</sup>	5 <sup>a</sup>	5 <sup>b</sup>	3
New onset seizure. ETOH, and/or drug related.	7 <sup>c</sup>	8 <sup>c</sup>	6 <sup>c</sup>	5 <sup>c</sup>	2	2	2	2	2
New onset seizure. Aged 18–40 years.	8 <sup>c</sup>	7 <sup>c</sup>	6 <sup>c</sup>	5 <sup>c</sup>	4	4	2	2	2
New onset seizure. Older than age 40.	7 <sup>c</sup>	8 <sup>c</sup>	3 <sup>c</sup>	5 <sup>c</sup>	4	4	2	2	2
New onset seizure. Focal neurological deficit.	8 <sup>c</sup>	8 <sup>c</sup>	7 <sup>c</sup>	6 <sup>c</sup>	3	3	2	2	2

Rating Scale: 1, least appropriate; 9, most appropriate.

<sup>a</sup> May be helpful in pre-op planning.

<sup>b</sup> Data probably equivalent to BOLD and SPECT.

<sup>c</sup> In the acute or emergency setting, CT may be the imaging study of choice.

(fMRI), have contributed to the presurgical evaluation of patients with epilepsy.<sup>18–20,23–41</sup>

Clinical PET with fluorodeoxyglucose (FDG) provides a measure of glucose uptake and thus metabolism. A seizure focus will typically manifest as a focus of hypometabolism on interictal (between episodes of seizure activity) examinations and will be seen as a focus of increased metabolism on ictal (during seizure) examinations. Interictal FDG-PET is sensitive (84%) and specific (86%) by electroencephalogram (EEG) criteria to temporal lobe epilepsy (TLE) and 33% sensitive and 95% specific to extratemporal epilepsy. By comparison, structural imaging by using a variety of MR field strengths and techniques yielded a sensitivity and specificity of 55% and 78%. SPECT utilizing perfusion agents such as 99mTc-HMPAO or 99mTc-Neurolite, as well as bolus MR imaging perfusion provide an assessment of regional cerebral blood flow rather than brain metabolism. A seizure focus will typically manifest as a focus of hypoperfusion on interictal examinations and will be seen as a focus of increased activity on ictal examinations. The utility of isolated interictal cerebral perfusion assessment in patients without anatomic imaging abnormality is limited.<sup>42,43</sup> The use of ictal/interictal subtraction imaging with coregistration on MR imaging and image-guided surgery datasets is proving to be more useful than interictal perfusion imaging alone.<sup>43</sup> Injection of the blood flow agent within 90 seconds of seizure onset does, however, appear to be required to demonstrate the expected localized increase in cerebral perfusion.<sup>44</sup> The use of perfusion techniques in epilepsy is therefore limited because of the technological challenge of injecting EEG-monitored patients within 90 seconds of seizure onset.

fMRI techniques include phosphorus and proton spectroscopy (MR spectroscopy), perfusion, and blood oxygen level dependent (BOLD) activation. The widespread application of most of these techniques in clinical practice depends on the widespread availability of high-performance MR imagers capable of performing fast echo-planar pulse sequences (EPIs), as well as substantial data postprocessing capabilities.

MR spectroscopy is a set of noninvasive techniques for in vivo chemical analysis of the brain, some of which can be performed on standard-performance clinical MR units. Although MR spectroscopy has been used extensively for the past 30 years in molecular physics and chemistry, its application to the study of epilepsy is relatively recent. Widely available proton and phosphorus single-voxel techniques have consistently demonstrated metabolite changes in the epileptogenic region

of the brain. MR spectroscopy or chemical shift imaging (CSI) allows simultaneous acquisition of spectra from all brain regions. The pictorial display of MR spectroscopy information facilitates comparison of the epileptogenic zone with the remainder of the brain and provides localizing information. CSI is not yet widely available in clinical practice. Initial studies suggest that both proton and phosphorus MR spectroscopy may be useful adjunctive presurgical tests for localizing seizure foci in patients with partial epilepsy, particularly in difficult cases, potentially reducing the need for intracranial-depth electrode EEG recordings and those with extratemporal seizure foci.<sup>19,25,26,32,33,35</sup>

Only magnetoencephalography (MEG) and EEG are capable of measuring epileptic brain activity directly and with high temporal resolution. The temporal resolution of PET, SPECT, and fMRI is poor by comparison (sec-min). Recent improvements in MEG technology now allow whole brain coverage and overlay of source information on MR or CT images (MSI). Available data indicate that interictal MEG can be an effective tool for localization of seizure foci, in patients with medically refractory partial epilepsy. Significant shortcomings include limited availability, high cost, and assessment limited to relatively superficial and tangential sources. Nonetheless, MSI does provide unique, accurate, and useful information about epileptogenic regions in the brain, and where available, has a potential role in the diagnostic workup of most patients with epilepsy.<sup>27,29,37,40</sup>

## Review Information

This guideline was originally developed in 1996. The last review and update was completed in 2006.

## Appendix

Expert Panel on Neurologic Imaging: John P. Karis, Principal Author, SW Neuro-Imaging, Phoenix, AZ; David J. Seidenwurm, MD, Panel Chair; Patricia C. Davis, MD; James A. Brunberg, MD; Robert Louis De La Paz, MD; Pr. Didier Dormont; David B. Hackney, MD; John E. Jordan, MD; Suresh Kumar Mukherji, MD; Patrick A. Turski, MD; Franz J. Wippold II, MD; Robert D. Zimmerman, MD; Michael W. McDermott, MD, American Association of Neurological Surgeons; Michael A. Sloan, MD, MS, American Academy of Neurology.

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