# *Imaging of Patients with Epilepsy*

*Peter E. Ricci, MD*

*Review of the roles of conventional computed tomography and magnetic resonance imaging in patients with epilepsy. Examination of the roles of fluorodeoxyglucose positron emission tomography in epilepsy patients. Introduce magnetic resonance spectroscopy and discuss its potential role in seizure imaging.*

*Introduction.* Prior to the advent of cross-sectional imaging, evaluation and classification of seizure patients was based on electroencephalography (EEG) data and clinical findings. Detection by EEG of abnormal electrical activity remains the definitive means to document the presence of epilepsy. However, classification of seizures based solely on EEG and clinical findings can result in the misclassification of some patients, particularly those individuals with partial seizures that rapidly generalize. With surgical cure rates routinely as high as 65 percent to 70 percent in patients with partial seizures that can be attributed to a morphologic abnormality, such misclassification is not acceptable.[1] Today, high-resolution computed tomography (CT) and magnetic resonance (MR) imaging play important roles in the evaluation and classification of seizure patients by virtue of their ability to identify epileptogenic lesions. In addition, the ability of MR imaging to thoroughly characterize lesion location and proximity to eloquent structures has greatly improved the surgical management of seizure patients. Physiologic imaging with single-photon emission computed tomography (SPECT), positron emission tomography (PET) and MR spectroscopy (MRS) have also had an impact on the evaluation and classification of seizure patients. However, their role in the routine evaluation of seizure patients is unclear.

*Objectives.* The objectives of this article are to: 1. Review the roles of conventional CT and MR imaging in patients with epilepsy; 2. Examine the role of fluorodeoxyglucose (FDG) positron emission tomography (PET) in epilepsy patients; and, 3. Introduce MR spectroscopy and discuss its potential role in seizure imaging.

*Computed Tomography.* CT is one of the most widely used imaging techniques for evaluating abnormalities of the central nervous system. Its widespread availability at emergent care facilities, high sensitivity detection of life-threatening lesions, and rapid scan time have made CT the most widely used imaging study for screening patients with new onset seizures. In a meta-analysis of epilepsy literature spanning 1988 to 1993, Greenberg and colleagues found that 26 percent of patients with new onset seizures have abnormal CT scans.[2] Based on their analysis, first-time seizure patients at high risk for significant intracranial pathology that would benefit from CT imaging were identified. High-risk individuals included those with a cancer history, age greater than 40, or current treatment with anti-coagulants; patients whose seizure was accompanied by head trauma, a focal neurological deficit, or persistent alternation in mental status were also found to be at high risk.

*Peter Ricci, MD, neuroradiologist, is on the Board of Directors of the Colorado Neurological Institute. Dr. Ricci graduated and did his Residency at Georgetown University School of Medicine. Dr. Ricci's areas of interest include the application of advanced MR techniques to the imaging of brain tumors and cerebral infarction.*

Despite its utility in the acute care setting, there are several drawbacks to CT that limit its use in epilepsy patients. Dense bony structures like the skull base create significant beam-hardening artifacts that make evaluation of the inferior frontal and temporal lobe structures difficult. CT can only image the brain in the axial or oblique axial plane, which significantly limits its ability to characterize lesions. Sensitivity of CT for acute stroke detection (one of the leading causes of new onset seizures in the elderly) is also limited. Because of these and other limitations, there is little role for CT in the evaluation of chronic epilepsy. Its principal role remains triaging patients with new onset seizures, particularly those at high risk.

*Magnetic Resonance Imaging.* Since the mid-1980's, when it became widely available for clinical use, MR imaging has been the preferred platform for evaluating diseases of the brain and spinal cord. Its advantages over CT are numerous and include superior contrast resolution, the ability to image the brain in multiple planes (axial, sagittal, coronal, and oblique), and the absence of beam-hardening artifacts. These advantages result in better detection of small lesions, improved differentiation between gray and white matter structures, and better visualization of the hippocampus, all of which are critically important in epilepsy imaging. The sensitivity of MR imaging for detection of epileptogenic lesions, such as tumors, vascular malformations, and mesial temporal sclerosis, has been estimated to be between 90 percent to 100 percent.[3] Detection of neocortical sclerosis secondary to small ischemic injuries, trauma, or infection is less robust, ranging from 80 percent to 90 percent.[3] In addition, MR imaging has been shown to have significant prognostic value for predicting the likelihood that a patient will be seizure free following epilepsy surgery. Overall, MR imaging is the preferred imaging tool for detecting the structural abnormalities that can result in seizure activity.

MR imaging protocols vary widely between institutions, reflecting differences in physician preference, scanner capability and patient population. Our general MR imaging protocol at the Colorado Neurological Institute includes a sagittal T1-weighted spin-echo localizer, axial T2-weighted fast spin echo (FSE) and fast FLAIR sequences, and an axial high-resolution T1-weighted gradient-echo volume acquisition. However, because the most common etiological substrates of epilepsy vary with age, MR imaging studies must be tailored to the patient's age and most likely diagnosis. For example, in patients with EEG documented temporal lobe epilepsy, an oblique coronal high resolution FSE T2 weighted series oriented perpendicular to the long axis of the hippocampus is required to detect changes in the hippocampus and other mesial temporal structures. Congenital malformations (eg, cortical dysplasia, heterotopia, lissencephaly, and schizencephaly) are the most common identifiable cause of seizure activity in children; therefore, we use an inversion-recovery prepped T1-weighted 3D-FSPGR high-resolution sequence that maximizes gray-white differentiation to enhance the detection of such lesions. In teenagers and young adults, trauma is the most common cause of epilepsy, necessitating use of a T2-weighted gradient echo sequence designed to detect evidence of recent or remote hemorrhage. After age 60, cerebrovascular and neoplastic diseases are the most common causes of epilepsy making the use of diffusion imaging and intravenous contrast agents mandatory. Patients in whom seizures are associated with an acute neurological deficit also require a diffusion study, regardless of their age.

The benefit of an MR exam tailored to the most likely diagnosis is highlighted by 2 of the more common causes of epilepsy; mesial temporal sclerosis (MTS) and neuronal migration disorders. Mesial temporal sclerosis is the most common cause of temporal lobe epilepsy, accounting for 85 percent of cases. The histological hallmarks of MTS, neuronal cell loss and gliosis, can involve the hippocampal head (88 percent of patients), body (61 percent), or tail (51 percent). The MR imaging correlates of those histological changes are hippocampal volume loss and architectural distortion (secondary to neuronal cell loss), and increased signal on T2-weighted images (due to gliosis). However, detection by standard MR imaging is difficult due to the small size of the hippocampus (normally 1.5 to 3.5 cc) and the small differences that can occur normally (right hippocampus can be 0.6 cc larger than the left while the left should be no more than 2 cc larger than the right). Diagnosis therefore requires a high-resolution sequence capable of detecting such minor changes. At the CNI, we use a 3 mm thick high resolution T2-weighted FSE oblique coronal sequence oriented perpendicular to the long axis of the hippocampus. Hippocampi are then visually assessed for decreased size, abnormally high signal intensity, and architectural distortion *(Figures 1 and 2).* At some institutions, hippocampal volumes are determined in order to detect even more subtle volume loss. Extra-hippocampal changes, such as atrophy of mammillary body, amygdala, column of the fornix, and parahippocampal white matter can also be seen with MTS *(Figure 1)*. Dilatation of the temporal horn adjacent to the hippocampus is generally not a reliable indicator of hippocampal pathology.

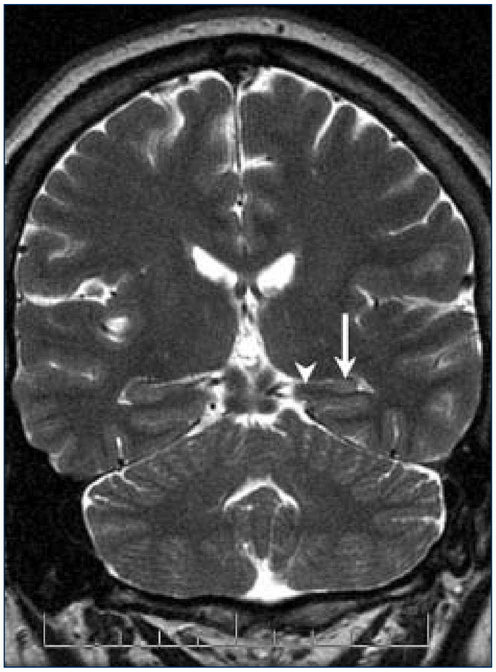

*Figure 1*

*Figure 1.*
High-resolution coronal T2-weighted image demonstrates the classic imaging changes of mesial temporal sclerosis. The left hippocampus (solid arrow) is smaller than the right and exhibits subtle architectural distortion. These changes correlate with neuronal volume loss on histopathological studies. The white matter volume in the left paraphippocampal gyrus (solid arrow head), a secondary sign of MTS, is also decreased.

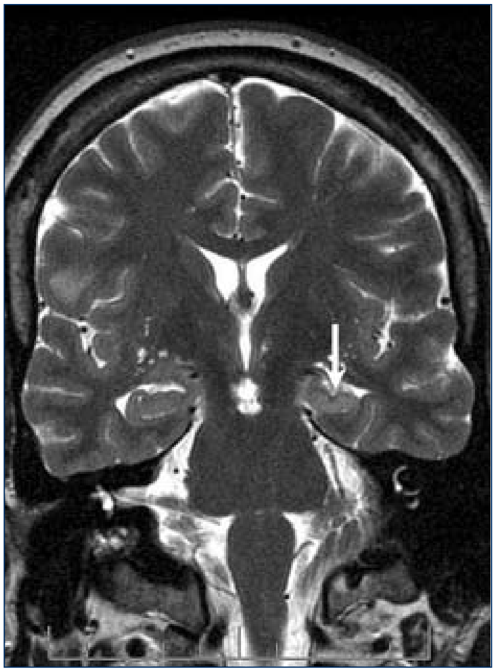

*Figure 2*

*Figure 2.*
High-resolution coronal T2-weighted image demonstrates subtle increased signal in the left hippocampus (solid arrow) compared to the normal right side. The increased signal likely reflects gliosis that occurs in response to hippocampal injury. Axial images typically cannot detect such subtle changes.

Imaging of neuronal migration disorders requires a different imaging paradigm than mesial temporal sclerosis.

*Figure 3a.*

Axial T2-weighted FLAIR image demonstrates small nodular foci lining the ependymal surface of the lateral ventricles bilaterally.

*Figure 3b.*

Axial inversion-recovery 3D FSPGR image optimized for gray matter - white matter differentiation better depicts the extent of the bilateral nodular heterotopia. The identical signal intensity of the nodules and cortical gray matter confirms the diagnosis.

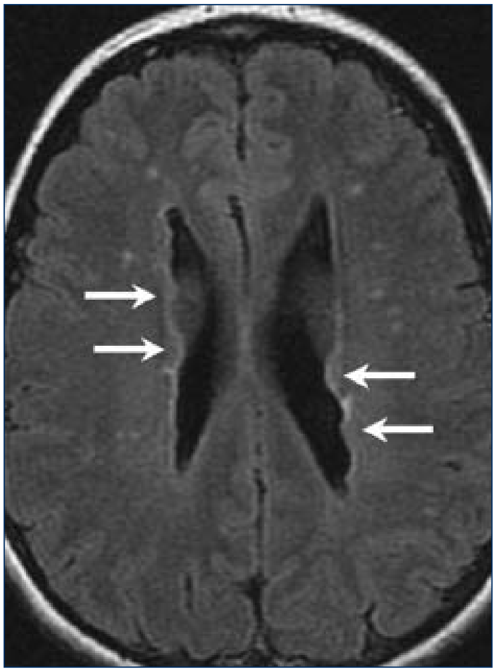

*Figure 3a*

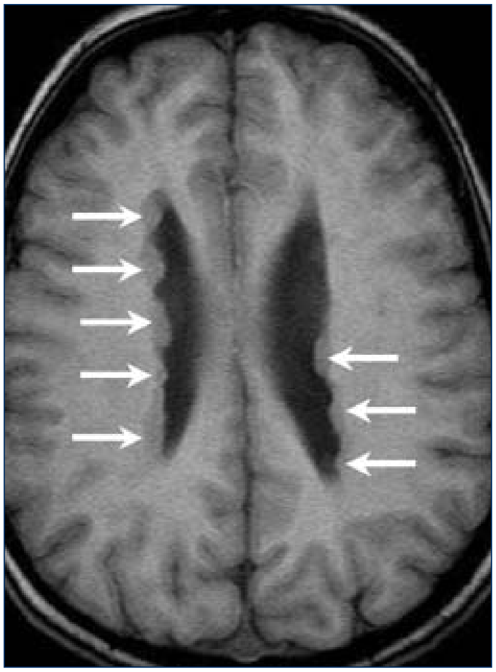

*Figure 3b*

Normal cortical development occurs in 4 stages: stem cell proliferation in the germinal matrix, differentiation of stem cells to mature cells, cellular migration outward to the cortex, and cortical organization. Depending on the stage at which this process is disrupted, a variety of migration disorders can result. To diagnose migration abnormalities, high-resolution imaging in which differentiation between gray and white matter structures has been optimized is essential. At the CNI, we use an inversion-recovery prepped volumetric T1-weighted FSPGR sequence in which the imaging data is partitioned into 2.5 mm thick slices. The inversion-recovery pulse suppresses signal from gray matter, effectively maximizing contrast differentiation between gray and white matter. *Figure 3* illustrates how this sequence improves detection of heterotopic gray matter.

*Nuclear Medicine Techniques.* While the role of MR imaging in epilepsy is clearly established, the roles of PET and SPECT imaging are not, even though both techniques predate MR imaging. This is due in part to their inability to depict structural abnormalities as clearly as MR imaging. In addition, PET imaging is also limited by scanner availability and cost. Certainly, conflicting results of PET studies in the medical literature have contributed to the confusion, and were part of the reason the Health Care Finance Administration concluded that there were insufficient data to draw conclusions on the role of PET imaging in epilepsy surgery.[4]

The primary agent used for PET imaging in epilepsy is fluorodeoxyglucose (FDG), a glucose analog that detects regional differences in glucose metabolism. In general, both mesial temporal sclerosis and neocortical sclerosis produce regions of hypometabolism on FDG PET studies. However, the hypometabolism is not specific with regard to underlying etiology (one of the major advantages of MR imaging). Imaging studies

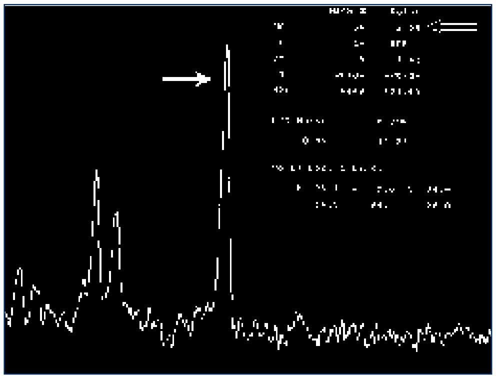
*Figure 4a*

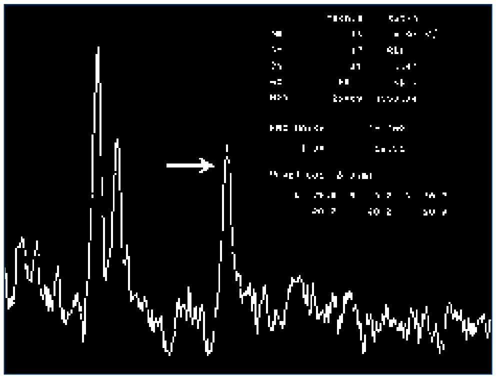
*Figure 4b*

*Figure 4a.*

Single-voxel MR spectrum from a normal hippocampus demonstrates normal NAA (solid arrow) and Cr peaks (small peak to left of NAA). The NAA/Cr ratio of 2.64 (open arrow) is also normal.

*Figure 4b.*

Single-voxel MR spectrum from a patient with MTS reveals a marked decrease in NAA signal (solid arrow) and NAA/Cr ratio, indicating significant neuronal volume loss.

comparing PET and technicium-99m SPECT imaging have demonstrated the superiority of FDG PET, particularly when compared with inter-ictal SPECT. Studies comparing PET and MR imaging are less conclusive, with numerous published studies indicting the superiority of both MR imaging and PET.

The primary role of FDG PET imaging at present is to evaluate patients that meet the following criteria: chronic epilepsy that is refractory to medical therapy, inconclusive MR imaging, and EEG evidence of a defined seizure focus. Demonstration of hypometabolism that correlates with EEG changes in those patients supports a diagnosis of MTS or neocortical sclerosis. Unfortunately, the extent of the FDG PET abnormality may not correlate with the extent of histological changes, making surgical planning difficult. Furthermore, the decision to proceed with surgery is a difficult one in light of studies that have demonstrated poorer outcome when the MR imaging is normal. Invasive monitoring with depth electrodes and cortical grids should be considered if surgery is contemplated in epilepsy patients with a negative MR scan.

*Magnetic Resonance Spectroscopy.* MR spectroscopy is a relatively new technology used in the evaluation of central nervous system diseases. Unlike the anatomic pictures of conventional MR imaging, MR spectroscopy produces "spectra", or chemical maps which reflect the relative quantities of various products of cerebral metabolism *(Figure 4a)*. Like PET imaging, it provides a non-invasive assessment of cerebral metabolism. Metabolites detected by MR spectroscopy include N-acetyl aspartate (NAA, a marker of neuronal viability), creatine (Cr) and phosphocreatine (intermediaries in cellular energy metabolism), choline (Cho) containing compounds (cell membrane precursors), glutamine and glutamate (neurotransmitters), myo-Inositol (a glial cell marker), and lactate (a by-product of anaerobic glycolysis). Advantages over other physiologic techniques include wider availability than PET scanners, greater latitude with the time of scanning than ictal SPECT studies, and better accuracy than inter-ictal SPECT studies for temporal lobe epilepsy. However, its role in epilepsy imaging at this time remains unclear.

In patients with suspected MTS, MR spectra have been shown to exhibit decreased NAA in the involved hippocampus in greater than 90 percent of patients; this is believed to correspond to the neuronal volume loss seen histologically. NAA/Cr and NAA/Cho ratios are diminished, largely due to the decreased NAA *(Figure 4b)*. Some studies have also demonstrated an increase in Cho signal, which may reflect the reactive gliosis that occurs with MTS. In the post-ictal period, lactate is often elevated. In one study, MR spectroscopy and FDG PET results were concordant with MR imaging on the side of hippocampal abnormality in 85 percent of cases. False lateralization rates for spectroscopy and PET in that study were 3 percent to 6 percent, respectively.[5]

*Conclusion.* Cross-sectional imaging studies play a significant role in the evaluation of epilepsy patients. The primary goal of imaging is to non-invasively detect and localize epileptogenic lesions that would be amenable to surgical treatment. MR is the imaging modality of choice for patients with epilepsy due in large part to its high sensitivity for detecting mesial temporal sclerosis in temporal lobe epilepsy patients, and its superior sensitivity for vascular abnormalities, tumors, and infarcts compared with CT. Ultimately, metabolic analysis of the brain with MR spectroscopy may prove to be more sensitive than conventional MR imaging, but more thorough investigation is still needed before it can be implemented universally.

*Address comments and questions to:*
Peter E. Ricci, MD
Section of Neuroradiology
Swedish Medical Center
501 E. Hampden Avenue
Englewood, CO 80113