Epilepsy imaging: Approaches and protocols

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n epileptic seizure is defined as "an excessive burst of abnormally synchronized neuronal activity affecting small or large neuronal networks that results in clinical manifestations that are sudden, transient, and usually brief."1 Epilepsy is characterized by recurrent seizures secondary to a predisposition to generate abnormal electrical discharges from cortical grey matter, and is complicated by subsequent neurobiological, cognitive, psychosocial and occupational consequences. Up to 10% of the population will have at least one seizure in their lifetime, but only about 2% of the population will develop epilepsy. Seventy million people in the world have epilepsy, with between 34 and 76 new cases per 100,000 diagnosed every year.² The annual incidence of epilepsy in the U.S. ranges between 15 and 71 per 100,000 person-years.³ In general, children and elderly individuals have a

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higher incidence of epilepsy than young and middle-aged adults.³ Fortunately, 70% of these cases are controlled by anti-epileptic medications. However, the remaining 30% of those with epilepsy have drug-resistant seizures.⁴ Functional neurosurgery offers a potential cure to these patients if the seizure focus can be localized and safely resected. Imaging, therefore, is critical to potentially identifying the etiology of seizure activity and to guiding therapy.

Seizures are classically defined as either generalized or partial (Table 1). Essentially, in generalized seizures the onset is global and with partial seizures the onset is focal. Both generalized and partial seizures are more common in children than in adults.⁵ Overall, the incidence of partial seizures is greater than primary generalized seizures. With generalized seizures, there is an immediate loss of consciousness, sometimes accompanied by generalized convulsions not localizing to a specific anatomic location and without recollection of the event.⁶ Structural lesions are less likely to be discovered with primary generalized seizures (eg, in childhood absence epilepsy), but are very common with par-

Table 1.				
Seizure type		Clinical features		
Generalized		Immediate loss of consciousness +/- generalized convulsions without localization Structural lesion less common		
	Simple	Focal onset mapping to anatomic area Can secondarily generalize Underlying lesion more common		
Partial	Complex	Partial seizure with loss of consciousness Can secondarily generalize Temporal lobe most common, but can also arise from any neocortical area		

Table 2.				
Patient age	Chronicity	Common causes	MR imaging protocol	
Pediatric	New	Infection Venous infarction Metabolic abnormalities Structural lesions (less common)	Basic MR brain imaging MRV/CTV Post contrast FLAIR	
	Chronic	Cortical dysplasias Heterotopic grey matter Phakomatoses Cavernous malformations Low-grade tumors MTS (after age 10)	T2* GRE volumetric T1 with multiplanar reconstructions	
Adult	New	Infection (younger patient) Prior trauma (younger patient) Remote infarct (older patient) Malignancy (older patient)	T2* Post contrast FLAIR	
	Chronic	MTS Cavernous malformations Cortical dysplasia Neoplasm	Cor T2 Cor T2* Cor T2 FLAIR Cor GRE volumetric T1 with multiplanar reconstructions Prior trauma or infarction	

tial seizures. Partial seizures demonstrate focal onset such as auras or focal motor symptoms mapping to a specific anatomic area or areas.⁶ Partial seizures are further characterized as simple, where consciousness is preserved, or complex, where there is loss of consciousness. Rapid secondary generalization of partial seizures can occur, sometimes confusing the clinical picture.

Magnetic resonance imaging is the modality of choice to evaluate the structural etiology of a seizure and to assess the potential need for surgery. Computed tomography may be the study of choice in an emergent situation. It is vital to consider patient demographics, such as age and clinical history (including a history of malignancy), as well as type and chronicity of seizure activity, to address the most common and critical etiologies in the imaging protocol design (Table 2).

Resources are best used when new seizure patients are triaged to routine screening brain imaging protocols, while refractory epilepsy cases should undergo more detailed, high-resolution protocols. When designing the MRI protocol, it is important to recognize the superiority of 3T to 1.5T MR imaging, which includes increased contrast-to-noise ratio, as well as spatial and anatomic resolution. ^{7, 8} Depending on the expected common pathologic entities in a particular demographic group, certain MRI sequences may be added to increase diagnostic yield. With a new-onset seizure, the imaging priority should be focused on ruling out an acute process, rather than visualizing a subtle epileptogenic focus. For example, venous infarction related to dural venous sinus thrombosis may be the suspected underlying cause of a new-onset seizure in the pediatric population; thus, an MR or CT venogram should be performed.



FIGURE 1. Pediatric new seizures, pneumococcal meningitis. MRI in this 5-month-old boy shows extensive pia-arachnoid membrane enhancement (white arrows) as well as linear diffusion restriction, compatible with inflammatory cellular material, characteristic of meningitis. The subdural space shows complex inflammatory adhesions and reactive fluid (suppressed on FLAIR and dark on DWI, so not empyema), with overlying dural enhancement (red arrows). The brain parenchyma is normal.



FIGURE 2. Pediatric new seizures, nonaccidental trauma. 2-year-old with somnolence and then new seizures. Initial CT shows convexity and falcine subdural blood (red arrows) and multiple fractures (latter not shown). Follow-up MRI at 3 days shows right hemisphere swelling and diffusion restriction in a nonvascular "holo-hemispheric" pattern. This appearance may represent a combination of ischemia, metabolic damage from prolonged seizures and excitotoxic-mediated cellular injury.



FIGURE 3. Pediatric new seizures, venous sinus thrombosis. This 4-year-old girl on chemotherapy for leukemia shows extensive right hemisphere swelling and heterogeneous hemorrhage, with a filling defect ("empty delta" sign, horizontal arrow) in the superior sagittal sinus on contrast-enhanced CT. Follow-up MR confirms methemoglobin clot in the sinus, and no flow on 3D phase-contrast venography (oblique arrows). Seizures are commonly observed with venous infarction at presentation, but are much less common with acute arterial infarction. This patient recanalized her sinuses and made a full neurologic recovery

In individuals with epilepsy, thin-section 3D coronal oblique T1 gradient echo and coronal oblique T2 series are added to assess for more subtle abnormalities, including hippocampal sclerosis or cortical dysplasias. High-resolution 3D sequences and T2 FLAIR (FLuid Attenuated Inversion Recovery) images increase the sensitivity to subtle cortical dysplasia and other abnormalities, including neoplasms.⁹ Our goal here is to provide an efficient and practical imaging approach to evaluating children and adults with seizures of all types.

New-onset seizures: General considerations

For the 10% of individuals who experience a seizure their lifetime, the majority (two-thirds) will represent a new-onset, nonrecurring seizure.¹⁰ Peak prevalence is bimodal (< 1 yr and >55 yrs of age). The imaging approach is driven by empiric observation of the most common and critical etiologies of seizures, which varies by age of presentation.

Pediatric new seizures

New-onset seizures represent the most common neurologic emergency of childhood, with approximately 4-10% (150,000) of children and adolescents per year presenting for evaluation of a newly occurring seizure disorder.¹¹ Only 20% of these patients will go on to develop epilepsy. Screening MRI examination of the brain, with or without contrast, is typically adequate to evaluate the broad differential in these patients, with important exceptions in the setting of neonatal seizure and venous thrombosis, as detailed below. Specialty sequences needed to uncover subtle cortical abnormalities, such as thin-section 3D gradient echo T1 with multiplanar reconstruction, should be generally reserved for patients with chronic epilepsy (Table 2).

The most frequently occurring condition associated with acute seizures in children is a febrile illness, with febrile seizure representing a unique entity in the pediatric population.¹¹ Most patients present with "simple" febrile seizures,



FIGURE 4. Adult new seizures, herpes simplex virus type 1 (HSV-1) encephalitis. This 35-year-old man presented with headache, nausea, vomiting and confusion. MRI shows regional edema in a distribution characteristic for HSV-1: anterior-medial temporal, insular, and subtle cingulate gyrus changes (arrows), with heterogeneous diffusion topography (some areas restricted, others iso-intense or vasogenic). HSV-1 is the most commonly identified sporadic encephalitis in adults, and proven here by PCR from spinal fluid. He was treated with acyclovir and made a full recovery.



FIGURE 5. Adult new-onset seizures, arterial infarction from cardiac embolism. This 21-yearold presented with new left-sided focal seizures. MRI done at 2 weeks shows focal right frontal gyral T2 hyperintensity and enhancement, with isointense signal on DWI, characteristic of a subacute infarction. Despite imaging findings strongly suggestive of infarction, she underwent biopsy, which confirmed infarction in this atypical presentation. Grey matter injury from prior infarction often leads to delayed onset seizures, usually a year or more after the event, and is a common cause of new seizures in the elderly.



FIGURE 6. Adult new-onset seizures, metastatic carcinoma. This 62-year-old man presented with headaches and left hemiparesis, followed by seizures. MRI shows mutilifocal enhancing lesions. Postcontrast T2 FLAIR images built into a basic brain MRI protocol are complimentary to other series, and in some cases will show small superficial or leptomeningeal metastases better than high-resolution, gradient echo, T1-weighted images (arrow). Resection of the right frontal lesion revealed mucin-producing metastatic adenocarcinoma, with the primary site likely being gastrointestinal.

as defined by the American Academy of Pediatrics, and have been shown to carry no greater risk for having meningitis than those who have a fever without a seizure.¹²⁻¹⁴ However, a subset of "complex" febrile seizures, particularly in the instance of febrile status epilepticus, carries an increased risk of bacterial meningitis (12-18%).^{15, 16} Acute bacterial meningitis often presents with no or nonspecific imaging findings; however, if present, basic MRI with and without contrast is the most sensitive and specific modality. Findings can include abnormal leptomeningeal and pachymeningeal enhancement, abnormal cortical FLAIR signal, diffusion restriction, and/or hydrocephalus (Figure 1). In cases of suspected meningitis, a subtle communicating hydrocephalus may be the only imaging sign at presentation, so careful evaluation for dilatation of the temporal horns and third ventricle is required. Ultimately, diagnosis of meningitis relies on cerebrospinal fluid sampling.

For new-onset pediatric seizure patients presenting without fever, basic MRI examination is the preferred examination for work-up.^{17, 18} Intracranial masses are less likely to be a cause of acute seizures in pediatric patients than in adults, as the majority of childhood CNS tumors occur in the posterior fossa, without the supratentorial cortical involvement typically implicated in seizure activity.

A special consideration in the setting of pediatric new-onset seizure is that of the neonate, in which presentation can be more clinically subtle but is often associated with significant morbidity and mortality, highlighting the need for rapid and thorough etiologic evaluation.¹⁹ Ninety percent of full-term newborns have an identifiable cause for their seizure, the most common of which is hypoxic-ischemic encephalopathy.14 Central nervous system infection and intracranial hemorrhage (birth trauma, prematurity, non-accidental trauma) are additional important considerations, as are congenital intracranial structural abnormalities and



FIGURE 7. Adult new-onset seizures, post-traumatic. This 40-year-old man reported an episode of severe blunt head trauma as a child, but had no seizures until nearly 30 years later. MRI shows evidence for bifrontal encephalomalacia with tissue loss, gliosis by FLAIR, and hemosiderin deposition on the brain surface (arrows). Gradient echo T2* or susceptibilityweighted imaging sequences are key to detecting old blood products. Seizures are a common delayed complication of many brain injuries, including trauma, infection and remote infarction.



FIGURE 8. Pediatric epilepsy, Sturge-Weber Syndrome. A 12-year-old girl with classic imaging features, including right hemisphere atrophy, mineralization on T2* sensitive series, extensive pial angioma, and slow flow on perfusion-weighted images (PWI; FMT=first moment transit time). Multiplanar reconstructions from the volumetric postcontrast T2 FLAIR (arrows) often show the meningeal and choroidal angiomas lesions better than traditional T1-weighted series.



FIGURE 9. Pediatric epilepsy, tuberous sclerosis. 2-year-old boy with frontal white matter radial migration lines, insular and occipital cortical tubers, and subependymal nodules (arrows). Note the subependymal nodules show signal characteristics of mature white matter, distinguishing these lesions from grey matter subependymal heterotopia.

metabolic derangements, particularly hypoglycemia (Figure 2). Emergent neuroimaging may be appropriate in this setting. Though ultrasound is valuable, CT is superior at delineating the extent of intracranial hemorrhage, cortical abnormalities, and other emergent conditions. When rapidly available, and in the setting of clinical stability, basic MRI of the brain can offer even more detail, and can adequately assess the described potential causative entities.¹⁷

While basic MRI sequences of the brain are sufficient to diagnose most pathology, an exception is in the evaluation of intracranial venous structures. Cerebral venous thrombosis (CVT) leading to infarction can present acutely as seizures, with more than half of those patients representing neonates. 20, 21 The pathoetiology of CVT is diverse: Asphyxia and difficult delivery are specific to neonates, while dehydration, prothrombotic disorders and infections of the head and neck affect newborns and older children.²¹ Diagnosing CVT and its complications requires a high degree of clinical suspicion, close inspection of the intracranial venous system, and knowledge of common venous infarct patterns. Dedicated venous imaging, such as noncontrast time of flight (TOF) MRV, contrast-enhanced MRV, and contrast-enhanced CTV assist greatly in the diagnosis (Figure 3). One imaging pitfall of CVT is that the normal flow gaps in the neonatal venous sinuses can mimic occlusion. This particularly affects the posterior aspect of the superior sagittal sinus, and may be related to smaller caliber of the sinus, smaller venous flow, and/or skull molding.²⁰

Adult new seizures

The etiology of new-onset seizures in the adult population has a limited differential which can be narrowed by patient age. Leading considerations include infection or prior trauma in a younger patient and remote infarction or malignancy in an older patient (Figures 4-6). Imaging of these patients is fairly straightforward, with basic



FIGURE 10. Malformations of cortical development. (A) During the first trimester, immature neurons proliferate and are then selectively pruned down in the germinal zone at the margins of the developing fetal ventricle. (B) Surviving neurons destined for the cortex subsequently migrate outward in radial fashion along radial glial guide fibers (red cells on purple fibers). A small but important subset of mostly GABA-ergic neurons migrate from the ganglionic eminences in the subpallidal region along tangential pathways through the developing cortex (blue neurons and pathways). (C) Neurons reaching the cortex are laid down into a well-organized, 6-layered, adult-type cortex, which subsequently folds and organizes further from term to early infancy. Malformations may occur due to disruption or arrest of these complex processes at any stage, leaving potentially epileptogenic grey matter in an abnormal location, producing characteristic MRI patterns such as: (D) periventricular nodular heterotopia; (E) band heterotopia "double cortex sign;" or (F) schizencephaly with polymicrogyria. Figure and conceptual approach gratefully adapted from the work of Jim Barkovich, MD.



FIGURE 11. Adult epilepsy, dysembryoplastic neuroepithelial tumor (DNET). This 20-year-old woman presented with longstanding medically refractory partial epilepsy. There is a complex, multicystic, T2-hyperintense mass centered in the right amygdala (arrows) (non-enhancing on other series, not shown). Findings are classic for DNET, with longstanding refractory seizures and a "soap bubble" appearance to the mass. Surgery is often curative in these indolent, low-grade tumors, which seem to be inherently epileptogenic.

pre- and postcontrast MRI sequences for diagnosis. A helpful protocol addition is postcontrast FLAIR imaging, which increases sensitivity to leptomeningeal spread of infection and neoplasm.²² Evidence of prior trauma should be closely sought for in the typical locations, including the anteroinferior frontal and temporal lobes. Multiple small foci of T2* susceptibility suggestive of diffuse axonal injury also may implicate

Table 3.

Malformations due to abnormal neuronal and glial proliferation

- 1. Microlissencephaly
- 2. Hemimegalnecephaly
- 3. Cortical focal cortical dysplasia (including balloon cells)

Malformations due to abnormal neuronal migration

- 1. Lissencephaly
- 2. Gray matter heterotopia: periventricular or subcortial (laminar)

Malformations due to abnormal cortical organization

- 1. Polymicrogyria
- 2. Schizencephaly
- 3. Cortical dysplasia (no balloon cells)

trauma as an etiology for new seizures in an adult (Figure 7).

Epilepsy: General considerations

After experiencing a first seizure, the recurrence risk of a subsequent seizure is approximately 25-50%. The risk of additional seizures increases after two seizures, and therefore, antiepileptic drug therapy is typically instituted after the second seizure.¹ As previously discussed, the challenge in epilepsy imaging is to identify the most likely and most important potential pathologies in each patient based on age, clinical history and type of seizure activity, in order to best direct the imaging resources and protocols.

Seizures that generalize at their onset usually do not have a focal pathologic lesion. Partial seizures (with or without secondary generalization) or medically refractory cases tend to yield more findings by MRI. In infancy and childhood, inborn errors of metabolism and developmental disorders such as neuronal migration anomalies and neurocutaneous syndromes predominate as identifiable causes. In patients with medically refractory epilepsy, particularly of the complex partial type, mesial temporal



FIGURE 12. Adult epilepsy, right mesial temporal sclerosis. A 51-year-old man with chronic refractory complex partial epilepsy. There is focal atrophy and abnormal T2 signal in the right hippocampus (red arrows). Note also the subtle volume loss and slight T2 signal changes in the adjacent white matter stem of the right temporal lobe, likely injury due to longstanding recurrent seizures. When postcontrast FLAIR is obtained as in this case, it is important not to confuse normal enhancing choroid plexus (horizontal white arrow, left side above the hippocampus) for true hippocampal signal change.



FIGURE 13. Pediatric epilepsy, focal cortical dysplasia type 2b. There is subtle blurring of the grey-white junction and slight grey matter thickening in the posterior frontal lobe (single red arrow) in this 4-year-old boy with medically refractory complex partial epilepsy. Subdural grids were implanted and the platinum electrode strands were localized on MRI (multiple red arrows), allowing confirmation of recorded ictal onsets co-localized to this subtle dysplasia. He has been seizure free following resection.

sclerosis is the most common imaging and surgical finding.²³

Pediatric epilepsy

Pediatric patients with chronic medically refractory epilepsy are affected with different pathology compared to patients with new-onset seizures and require specialized imaging. While patients with acute seizures can be adequately evaluated with a basic MRI exam, protocols for epilepsy should include high-resolution multiplanar imaging, including a coronal T1 3D GRE sequence. This sequence is particularly helpful when seeking to detect subtle structural abnormalities, such as cortical dysplasias, heterotopic grey matter, phakomatoses, cavernous malformations, low-grade tumors, and mesial temporal sclerosis.

Phakomatoses most commonly implicated in chronic pediatric epilepsy include tuberous sclerosis and Sturge-Weber Syndrome (Figures 8-9). ²⁴ Imaging findings characteristic of tuberous sclerosis consist of subependymal nodules, subependymal giant cell astrocytomas, white matter radial migration lines, and cortical and subcortical tubers. Approximately 98% of patients with tuberous sclerosis have subependymal nodules. Signal characteristics of these nodules are similar to mature white matter, differentiating these hamartomatous lesions from heterotopic gray matter, an additional developmental lesion implicated in chronic epilepsy. Further, subependymal nodules often calcify and do not grow. These imaging features distinguish nodules from the subependymal giant cell astrocytomas seen in 15% of patients with tuberous sclerosis (most commonly near the foramen of Monroe). Cortical and subcortical tubers are also common lesions in the setting of tuberous sclerosis, occurring in 95% of patients and most commonly located in the frontal and parietal lobes. The number of tubers correlates with the degree of the patient's neurologic impairment.²⁵

Abnormalities of cortical development are often associated with epilepsy, especially drug-resistant epilepsy. These cortical developmental anomalies can be grouped into three categories: 1) abnormal proliferation of neurons and glia; 2) abnormal migration of postmitotic neurons to the cortical plate; and 3) abnormal cortical organization and elaboration of connections.²⁶⁻²⁸ Table 3 lists many of the abnormalities of cortical development into these categories. Figure 10 illustrates the embryologic process of cortical development graphically, and demonstrates examples of the malformations associated with each category.

Adult epilepsy

Similar to pediatric patients, adults with epilepsy require more detailed MRI protocols. In addition to standard MRI pulse sequences, thin-section coronal T2, T1 3D GRE, and FLAIR sequences should be included to evaluate the temporal lobes. A high-resolution T1 3D GRE sequence (e.g. SPGR, MPRAGE, or BRAVO) is particularly useful for detecting subtle cortical dysplasias. Leading considerations in an adult with epilepsy include mesial temporal sclerosis, cavernous malformations ('cavernomas'), cortical dysplasias, neoplasm, and sequelae of prior trauma or infarction.²⁹ A T2* gradient echo sequence in the axial or coronal plane is necessary to evaluate for evidence of hemosiderin deposition related to prior trauma or cavernomas. Tumors should always be excluded in an adult



FIGURE 14. Chronic refractory complex partial epilepsy due to pathologically proven mesial temporal sclerosis. Coronal T2 images in this 15-year-old girl show very subtle atrophy and signal changes in the right hippocampus and temporal lobe white matter stem (red arrows). MRI co-registered with color-coded interictal 18-FDG-PET shows striking right temporal hypometabolism (white arrows), a reliable indicator of epilepsy localization.

with epilepsy, since even longstanding cases can harbor low grade neoplasms (Figure 11). While high-grade glial neoplasms and metastatic disease often present acutely with new onset seizures, lower grade malignancies such as ganglioglioma, pleomorphic xanthoastrocytoma, dysembryoplastic neuroepithelial tumor (DNET), and pilocytic astrocytoma often localized to the neocortical areas and can present clinically and radiographically similar to cortical dysplasias.

In medically refractory epilepsy patients, careful analysis for signs of mesial temporal sclerosis is undertaken, as it is the most common pathology found in these patients. The main radiologic findings of mesial temporal sclerosis are hippocampal atrophy, internal structural derangement and T2 hyperintensity; among these signs, atrophy is the commonest and most reliable (Figure 12). This condition is rare before the age of 10 yrs. While the pathogenesis is unknown, it may be related to prior infection or febrile seizures as a child. This condition is characterized by hippocampal atrophy and gliosis best seen on coronal T2 FLAIR imaging as hippocampal volume loss with associated increased T2 signal and loss of grey white differentiation. Mass effect and enhancement are not seen with mesial temporal sclerosis. Imaging findings of mesial temporal sclerosis can be very subtle and evaluation of the ipsilateral amygdala, temporal lobe white matter stem, fornix, and mammillary body can be useful in detecting subtle cases.

Epilepsy is ultimately a functional grey matter disturbance, not a structural disease; it is therefore critical to recognize that any discovered imaging abnormalities need to be correlated with clinical seizure type and EEG features before causality is implicated. Care must also be taken not to confuse the transient post-ictal consequences of seizures (eg, PRES) as a cause of seizures. Proper evaluation of epilepsy requires a multimodality and multidisciplinary approach. PET scanning is useful in cases of neocortical epilepsy, where interictal hypometabolism corresponds to areas of concern. Electroencephalography and magnetoencephalography are additional noninvasive methods to localize seizure foci. Ultimately, invasive monitoring may be required if surgical intervention is considered (Figure 13). If surgery is considered, patients may undergo functional MRI (fMRI) imaging to map the proximity of seizure foci to areas of the brain associated with a specific function, such as speech and language, motor, or memory.

Multimodality 3D fusion techniques, such as fusing MR and PET images, allows for better anatomic correlation to areas of hypometabolism.³⁰ Areas shown to be abnormal or questionable by PET, SPECT, MEG, fMRI and spectroscopy studies can be coregistered to a common MR image set (Figure 14). This allows simultaneous comparison of the structural-functional relations among the various modalities. Using this approach, the areas where multiple modalities overlap are deemed as possible epileptogenic areas.

Increasingly available are fMRI techniques to help localize seizure onset. These methods are based on the MR detection of both cerebral blood flow effects as well as small shifts in the relative amounts of oxyhemoglobin vs deoxyhemoglobin in the vascular bed. As such, fMRI is typically limited to recording events occurring on the timeframe of seconds. Since epileptogenic spikes last just milliseconds, only very frequent ictal activity or longstanding interictal activity might be localized with fMRI. Nonetheless, several investigators have reported preliminary success using fMRI in epilepsy localization and characterization.31-33 Of particular interest, the ability to trigger the fMRI acquisition based on real-time EEG monitoring may provide a more detailed understanding not only of the areas involved in certain physiologic events, eg, focal epilepsy or cognitive processing, but also of the sequencing of the activation of the involved regions.³⁴ fMRI also affords the opportunity to perform noninvasive functional mapping to aid pre-operative planning. Such innovative fMRI approaches are likely to bring new insight into our understanding of the epileptogenic zone.

Conclusion

Evaluating patients with new-onset seizures and epilepsy requires a multimodality and multidisciplinary

approach. Imaging has a vital role in both identifying causative factors and guiding therapy. Clinical history and patient age, as well as type and chronicity of seizures, guide differential considerations and imaging protocol design. Imaging evaluation of new seizures employs basic MR imaging protocols, while epilepsy often requires more advanced imaging techniques, including multiplanar thin-section 3D MRI acquisitions, multimodality fusion and functional MRI.

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