

Imaging: Basic Structural MRI (Acquisition and Common Lesions)

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1) Indication for neuroimaging in new-onset seizures in acute and ambulatory outpatient settings:

The clinical presentation and setting dictates the options and appropriate follow up for neuroimaging in patients with new-onset seizures. Importantly, the clinical considerations and differential diagnosis of the etiology of new-onset seizures in the emergency setting differs from the outpatient ambulatory clinical setting, so the approach in each setting will be outlined.

In the emergency setting, immediate availability of the imaging modality takes first precedence. Logistically, CT is widely available in most hospitals and therefore often most appropriate for medically unstable patients. In an evidence-based review, Harden et. al. evaluated neuroimaging in emergency patients presenting with new-onset seizures.¹ In adults presenting to the emergency department, CT findings resulted in a change of acute management in 9 to 17% of patients.¹ CT abnormalities which changed acute management included traumatic brain injury, subdural hematomas, non-traumatic bleeding, strokes, tumors, and brain abscesses. In children presenting with first seizures (excluding simple febrile seizures), CT findings resulted in acute management changes only approximately 3 to 8% of patients. Frequent abnormalities which caused a change in acute management in pediatric subjects were cerebral hemorrhages, tumors, cysticercosis, and obstructive hydrocephalus. The predictive factors for finding abnormalities on CT included an abnormal neurologic examination, a predisposing history (i.e. a history of an illness or injury predisposing to epileptic seizures), or evidence of focal seizure onset. Because past studies in the emergency setting focus on the utilization of CT, there are no objective comparisons of CT vs. MRI in the emergency care setting.¹ While MRI is more sensitive in detecting brain lesions in epilepsy overall (as discussed below), there

are issues to consider in obtaining an MRI in the emergency care setting beyond availability and clinical factors. Often, MR imaging acquisition sequences in the emergency care setting are suboptimal and read as 'normal', which may delay future MRI studies with adequate acquisition parameters.

Overall, CT remains the most available neuroimaging modality in the acute care setting, and has impact on the clinical decisions for treatment. While not an absolute prerequisite, CT imaging is appropriate for subjects presenting with new-onset seizures in the correct clinical situation.

In the outpatient clinical setting, there are multiple studies examining neuroimaging in new-onset seizures.²⁻⁵ Early studies showed that CT imaging of subjects with new onset seizures revealed a lesion in approximately 12% of subjects.⁵ In contrast to the emergency setting, however, there are studies comparing CT and MRI in new-onset seizures in the outpatient clinical setting. In a study directly comparing 28 subjects with new onset epilepsy and positive MRI studies who also underwent CT at the time of presentation, only 12 of the patients undergoing CT showed a lesion.⁴ Importantly, of 15 subjects who presented with tumor on MRI, only 7 were detected on CT. Therefore, especially for patients who present with a negative CT when presenting with a first seizure, there is indication for follow up with an MRI scan.

One study of new onset seizures showed MRI abnormalities related to the cause of the seizure in 28% (177/764 subjects).² Of subjects with a lesion related to the seizure, findings were gliosis (46%), developmental abnormality (15%), cavernoma or AVM (15%), tumor (15%), and mesial temporal sclerosis (8%). Importantly, 20% of subjects (165/764) had coincidental lesions on MRI, not related to seizures, emphasizing the importance of clinical and EEG correlation of seizures with neuroanatomical characteristics of imaging findings. Overall, studies of new-onset seizures show associated MRI abnormalities in 14-48%.²

2) Imaging findings in chronic epilepsy:

Patients with pharmaco-resistant epilepsy who present to tertiary epilepsy centers for evaluation often undergo MRI acquisition to determine the etiology of their seizures, especially if previous imaging studies are reported as normal. Performing a high-quality epilepsy protocol MRI is important for evaluation for the etiology of epilepsy, and therefore clinical prognosis, as well as the possibilities of further treatment such as epilepsy surgery.

The importance of finding an MRI lesion is outlined by Semah et al⁶ who evaluated the response to medical treatment as related to the syndrome and MRI lesion in chronic focal epilepsy. The syndrome and etiology, and percent of subjects showing greater than one-year seizure freedom are as follows:

Cryptogenic focal epilepsy	45%
Symptomatic focal epilepsy	35%
Temporal lobe epilepsy	20%
TLE with MTS	11%
TLE without MTS	31%
Dual pathology (MTS+)	3%
Extratemporal focal epilepsy	36%
Cerebral dysgenesis	24%

A large study of 2000 referrals for MRI for seizures showed abnormalities in 20.2%.⁷ Of the 404 subjects who showed relevant abnormalities, findings were MTS (53.6%), cortical malformations (18.3%), vascular malformations (7.1%), tumors (5.1%), phacomatoses (1.5%), encephalomalacia or gliosis (9.6%), previous infarction (1.3%), encephalitis (0.8%), tuberculoma (0.3%), and encephalocele (0.3%).

The rates of lesion detection tend to go up in subjects with more severe epileptic seizures. In two studies of subjects with refractory epilepsy undergoing evaluation for epilepsy surgery, lesion detection rates were 82%⁸ and 86%.⁹

In cohorts which include older age groups, an MRI finding related to cerebrovascular disease is more common.¹⁰

3) Basic MRI acquisition parameters:

The clinically relevant findings of MRI depend heavily upon multiple parameters, some of which are not related to clinical factors. MRI acquisition parameters such as magnetic field strength, acquisition protocols, and expertise of the reader factor heavily into the final diagnostic yield of MRI.

MRI hardware has improved, allowing improved signal-to-noise ratios and greater spatial resolution. Studies comparing 1.5 T and 3.0 T scanners show

improved diagnosis of clinically significant structural lesions with 3.0 T scanners. Repeat scanning of patients undergoing evaluation for epilepsy surgery with a negative 1.5 T MRI yielded identification of a lesion with a 3.0 T MRI in 15 of 23 patients.¹¹ In 804 patients who underwent 1.5 and 3.0 T MRI studies, 3.0 T studies showed a relevant, new diagnostic finding in 5% of subjects. The most common new findings were hippocampal sclerosis, focal cortical dysplasia and dysembryoplastic neuroepithelial tumor.¹² Therefore, use of 3.0 T MRI scanners are preferred for epilepsy protocol studies. However, if 1.5 T studies are the only available option, optimization of the acquisition protocol remains important to enable the best detection of epilepsy-associated lesions.

There are several proposed MRI acquisition protocols, which have evolved with improvements in MRI hardware and software.¹³⁻¹⁶ The proper acquisition protocol insures high spatial resolution studies with the capability of detecting subtle MRI lesions. Based on recommendations for MRI acquisition from images of a large epilepsy surgery cohort¹³, Duncan et al.¹⁴ propose the following general acquisition protocol, describing which imaging sequences typically show different lesion categories.

- a) Three-dimensional volumetric T1-weighted imaging (1 mm isotropic voxels). This method provides excellent grey–white matter contrast and allows the assessment of cortical thickness and detection of malformations of cortical development. Images can be reformatted into any plane and post-processing techniques can be used to improve detection of abnormalities.
- b) T2-weighted imaging (axial and coronal). This imaging method allows assessment of hippocampal architecture and cystic tissue components of other lesions. The two orthogonal planes allow small lesions to be distinguished from partial volume effects, which are minimized by acquiring images orthogonal to the long axis of the hippocampus.
- c) Fluid-attenuated inversion recovery imaging (axial and coronal). This imaging method is sensitive to hippocampal sclerosis, focal cortical dysplasia, tumors, inflammation, and scars.
- d) T2* gradient echo or susceptibility-weighted imaging (axial). This method is sensitive to calcified and vascular lesions, such as cavernomas and arteriovenous malformations.

Scan interpretation

Proper image acquisition is of course a prerequisite for adequate scan interpretation. For example, subjective visual analysis of the hippocampus compares favorably to objective volumetric measurements of the hippocampus in detecting hippocampal sclerosis, if MR images are carefully and properly acquired.¹⁷

In addition to optimum image acquisition, the expertise of the reading physician plays an important role in scan interpretation. The sensitivity of focal lesion detection in subjects undergoing surgery was 39% for non-optimized image acquisition reported by non-experts, 50% for non-optimized acquisition reported by experts, and 91% for optimized acquisition reported by experts.¹⁸

4) Indications for CT and MRI:

As discussed above, CT has a role in evaluation of seizures in the emergency care setting. However, outside the acute care setting, MRI is almost always the preferable imaging modality for subjects with seizures and epilepsy. When comparing 117 patients who underwent surgery for medically refractory epilepsy, Bronnen et al⁹ found a sensitivity for detection of an abnormality in 95% for MR imaging and 32% for CT. In a subgroup of patients with solitary findings on post-surgical histopathology, MR imaging depicted an abnormality at the surgical site in 86% of patients compared to 28% for CT. Therefore, MRI is the overall indicated imaging modality in patients with chronic epilepsy, with the exception of obvious contraindications such as cardiac pacemakers, cochlear implants, and neurostimulators.

5) Role in prognosis in medical and surgical treatment of epilepsy:

Structural MRI findings associated with epileptic seizures play a role in the prognosis for treatment. As outlined above, the syndrome and MRI lesion in chronic focal epilepsy is predictive of response to treatment.⁶

In assessment for epilepsy surgery, co-localization of structural brain lesions with the epileptogenic zone as defined by EEG is important for favorable outcomes after epilepsy surgery. Awad et al¹⁹ evaluated epilepsy surgery subjects who underwent MRI and long-term intracranial EEG recordings. Outcome was analyzed in light of extent of resection of MRI lesions and/or EEG focus. Good postoperative outcome occurred in 17/18 (94%) in subjects with complete lesion

excision, regardless of extent of epileptogenic zone excision, 5/6 (83%) in subjects with incomplete lesion excision, but complete epileptogenic zone excision, and 12/23 subjects with incomplete excision of the lesion and epileptogenic zone. These results illustrate the importance of correlation of structural MRI and EEG findings in the evaluation of subjects for epilepsy surgery. Subsequent studies have confirmed the improved prognosis for seizure freedom after epilepsy surgery with MRI lesion resection.^{20;21}

Summary:

Structural neuroimaging plays a vital role in diagnosis and treatment of epilepsy. The appropriate neuroimaging study depends on the clinical situation, with CT often the appropriate test in the emergent care setting, and MRI almost always the test of choice in the non-emergent care setting. Neuroimaging findings depend heavily on the clinical situation in which obtained, with emergent onset seizures showing acute lesions, and chronic refractory epileptic seizures more often showing chronic lesions such as malformations of cortical development and hippocampal sclerosis. MRI acquisition parameters and the expertise of the interpreting physician play an important role in detecting structural lesions associated with epileptic seizures. Aside from detecting a lesion which requires treatment independently from the associated seizures (i.e. tumor or vascular malformation), establishing a structural imaging correlate of seizures also carries important prognostic value, as response to medical treatment is related to the epilepsy syndrome and MRI lesion. Finally, detection of a relevant structural MRI lesion in medically resistant epilepsy clearly enhances the possibility of favorable response to resective epilepsy surgery, and therefore plays an important role in assessing feasibility and prognosis in evaluation of patients for epilepsy surgery.

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