Neuroimaging In Epilepsy

A seizure is defined as a paroxysmal alteration in neurologic function due to excessive electrical discharge from the central nervous system. Epilepsy is defined as a condition of recurrent seizures, and medical intractability as recurrent seizures despite optimal treatment under the direction of an experienced neurologist over a two to three year period. Determining the underlying cause of a patient’s seizure is the fundamental goal in the workup of epilepsy. Imaging of the brain provides valuable information in this regard. The main purposes of neuroimaging in epilepsy patients are to identify underlying structural or metabolic abnormalities that require specific treatment and to aid in formulating a syndromic or etiologic diagnosis. Neuroimaging is even more important for those patients who have medically intractable seizures. Advances in technology to localize epileptogenic focus, especially with high resolution magnetic resonance imaging (MRI), have substantially improved the success of surgical treatment.

Common structural disorders associated with seizure and detected on imaging can be categorized into the following groups: hippocampal or mesial temporal sclerosis, cortical developmental malformations or neuronal migration disorders (cortical dysplasias, heterotopias, hemimegalencephaly, lissencephaly, schizencephaly, pachygyria, polymicrogyria, Rasmussen encephalitis), phakomatoses (Tuberous sclerosis, Sturge Weber syndrome, neurofibromatosis), vascular abnormalities (arteriovenous malformation, cavernous hemangiomas), infections (Tuberculoma, neurocysticercosis), neoplasms (ganglioglioma, dysembryoplastic neuroepithelial tumor, low grade gliomas and cerebral metastasis in adults), stroke, posttraumatic epilepsy, and miscellaneous conditions (gliosis, encephalocele).

The major utility of computed tomography (CT) scanning is in the initial evaluation of seizures, particularly in trauma, hemorrhage, infarction, tumors, calcified lesions and major structural changes. In perioperative patients, it is the imaging technique of choice as it can detect the bleed, hydrocephalus and assess electrode placement. However, the overall sensitivity of CT in patients with epilepsy is low (~ 30%), and because of poor resolution in the temporal fossa CT is of no use in detecting mesial temporal sclerosis, the most common pathology in intractable temporal lobe epilepsy.1

Magnetic resonance imaging (MRI), with its excellent spatial resolution, soft tissue contrast, and multiplanar capabilities, is the imaging modality of choice in investigating patients with seizure disorder. The sensitivity of MRI in identifying epileptogenic foci in patients with medically refractory patients has been reported to be more than 80%. However, in patients with idiopathic generalized epilepsy, MRI has not been shown to be useful. The correlation of the MRI finding with clinical and electroencephalography (EEG) findings are essential to avoid false positive localization of epileptogenic focus.2

Routine scanning protocol for a patient with refractory epilepsy may include axial or coronal T1 and T2-weighted imaging, Fluid-attenuated inversion recovery (FLAIR) imaging, and 3D volume acquisition sequences. Common 3D acquisition sequences include high resolution T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) and fast spoiled GRASS(3D-FSPGR), where GRASS is gradient recalled echo acquisition at steady state. T1-weighted sequences are used to define the brain anatomy, and T2-weighted or FLAIR sequences are used to detect the brain pathologies. High-resolution 3D volume acquisition provides good T1-weighted contrast between gray and white matter and helps to detect subtle cortical dysplasias and internal structure of hippocampus in case of mesial temporal sclerosis.3,4,5 For optimal assessment...

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of hippocampus the imaging should be in hippocampal axis (oblique coronal plane) with thin slices and good signal-to-noise ratio. The application of contrast agent is indicated if there is suspicious of primary or metastatic tumor, infection, or inflammatory lesion.

The specialized protocol includes Quantitative volumetry and T2 relaxometry, MR spectroscopy, Functional MRI (fMRI), Diffusion weighted imaging (DWI) & Diffusion tensor imaging (DTI), and Magnetic source imaging (MSI).

High resolution T1-weighted 3D volume gradient echo sequences are also used for quantitative measurement of volume of any particular region of interest. In the case of epilepsy this is usually the hippocampus. Volumetric analysis of the hippocampus can be performed both in adults and children with epilepsy, to detect more subtle volume deficits (atrophy) that may be missed by visual assessment alone. Volumetric measurements can be performed manually or with half-or fully-automated software, however, needs good knowledge of anatomical details. Longitudinal studies done to assess the progression of volumetric changes correlate with the seizure associated damage. T2 relaxometry is the quantitative determinant of the T2 relaxation time. To achieve this, several T2-weighted images are acquired at different echo times, and with these values an exponential decay curve is obtained to estimates the T2 decay rate of the imaged tissue. The tissues that have prolonged T2 are considered abnormal. In epileptic patients with hippocampal sclerosis, signal increase on T2-weighted images is typically observed in the hippocampus. The measured values of the hippocampal volume and the T2 times are correlated with each other, indicating that a marked volume loss is associated with a significant increase in T2 relaxation, reflecting the complex pathology of hippocampal sclerosis.

Proton MR spectroscopy (MRS) has proven to be a sensitive measure to detect metabolic dysfunction in patients with temporal lobe epilepsy (TLE), particularly mesial temporal sclerosis (MTS) involving hippocampus. 20% of patients with TLE have normal structural MRI scan and the findings in children generally tend to be more subtle than those in adults. MRS metabolite abnormalities may be found even in the absence of detectable structural abnormalities. NAA, NAA/Cho, NAA/Cr, and NAA/(Cho+Cr) all are decreased in atrophic hippocampi, as well as in nonatrophic hippocampi with abnormal EEG findings. Reduced N-acetyl-aspartate concentration suggests neuronal loss or dysfunction. TLE patients may also show increased choline and myoinositol signals, suggestive of gliosis. Studies of patients during or immediately after seizures (within 6 hours) may also show lactate increase in the epileptogenic focus. MRS also has promising role in the evaluation of patients with extratemporal epilepsy (frontal lobe epilepsy). In patients with structural MR evidence of malformations of cortical development (MCD) or neuronal migration disorders (NMD), MRS provides insight into both the pathology and true extent of the disease processes. Abnormally decreased NAA/Cr and Cho/Cr ratios have been noted in these lesions, as well as in the normal appearing brain contralateral to the lesion, when compared with gray and white matter of neurologic controls. MRS is of particular importance in patients with brain tumors. The characteristic elevation of choline makes MRS a valuable tool for the diagnosis of tumors and their differentiation from other lesions. There is also evidence that MRS can differentiate between tumor types. Neurotransmitter MRS studies have potential therapeutic impact in seizure patients. Glutamate and γ-amino-butyric-acid (GABA) can be measured using MRS editing techniques. Intracellular glutamate concentrations remain elevated in the epileptogenic hippocampus and neocortex, and contribute to the epileptic state by increasing cellular excitability.

Surgical treatment of refractory focal seizure has been an important and effective means for seizure control. However, the surgical outcome is dependant on precise localization of epileptogenic focus and functional areas of the brain. The functional MRI (fMRI), plays a very important role in preoperative localization of epileptogenic focus and assessment of cognitive function in patients with refractory epilepsy. During focal seizure, cerebral blood flow and metabolism is considerably increased. fMRI using blood oxygen level dependent (BOLD) technique can detect these cerebral hemodynamic changes. The excellent spatial resolution of fMRI helps to study cortical activation during epileptic activity and define epileptogenic focus in originally activated area. The recent development of EEG-triggered fMRI which allows interpretable electroencephalographic data to be recorded during MRI scanning, has advantage of combining the spatial resolution of imaging with the temporal resolution of electrophysiology in precise localization of seizure foci, thus increasing the rate of successful resection of the epileptogenic focus. The EEG-triggered fMRI is highly reliable, repeatable and noninvasive tool in localization of the seizure foci of patients with intractable focal seizure. Combined video-EEG and fMRI in localization of seizure foci has also shown good results. Long term epileptic activity in patients with epilepsy results in atypical distribution of cognitive function areas because of reorganization of cortical language and memory areas. Accurate localization of cognitive functional areas is necessary, to avoid their resection at the time of surgery, to modify surgical approaches for those patients at risk of language and memory deficit and to predict postoperative cognitive deficit after resection of seizure foci.

The diffusion-weighted signal reflects the molecular motion of water in the intra-and extra-cellular environments. In tissue components such as CSF, molecular motion is not restricted in any direction and is known as isotropic diffusion, detected by diffusion weighted imaging (DWI). In tissues with linear arrangement of myelinated fibers such as white matter tracts, the molecular motion is restricted to the axis along the white tracts and is known as anisotropic diffusion, detected by diffusion tensor imaging (DTI) or tractography. In epilepsy, DWI is used to assess acute cerebral ischemia, tumors or infections, while DTI has been used to assess the degree of distortion of white matter tracts in case of developmental abnormalities and other...
lesions responsible for seizure. Anisotropy is reduced in areas of structural abnormalities suggesting structural disorganization of white matter.17,18

Magnetoecephalography (MEG), also known as MSI when combined with structural imaging, has proved to be a new noninvasive tool for localization of epileptic focus. MSI is similar to EEG, but unlike EEG it detects magnetic rather than electric signal and is more accurate for localizing abnormal focus. It is increasingly useful for presurgical localization of epileptogenic lesions and stimuli induced normal neuronal function to minimize postoperative neurological deficits.19

Besides purely structural imaging techniques like MRI, functional imaging studies like interictal positron emission tomography (PET), and ictal and interictal single photon emission computed tomography (SPECT) may provide additional information in some patients and thus aid in clinical decision making. PET and SPECT are usually not indicated for the majority of patients with epilepsy but has important role in the surgical candidates. The detection of cryptogenic lesions is the main goals of functional epilepsy imaging with PET or SPECT. PET utilizes an injection of tracer 18F-labeled deoxyglucose (18 FDG) to measure brain metabolism. Interictal PET shows hypometabolism in the seizure focus, especially in TLE. Ictal PET is not practical due to extremely short half life of the radiotracers used. PET remains a diagnostic modality for presurgical localization of the focus in temporal lobe and extratemporal epilepsy when MRI is normal.20 SPECT utilizes injection of radio-labeled tracer Technetium99m hexamethyl-propyleneamineoxime (Tc-HMPAO) or ethyl cysteinate dimmer(Tc ECD), which has very slow distribution once in the brain. The tracer is stable for several hours, allowing delayed imaging. The most useful study for presurgical evaluation is an ictal SPECT, which usually reveals increased blood flow at site of seizure onset. Interictal studies often show relative hypoperfusion at the site of seizure onset. The substraction of the interictal from the ictal SPECT, and then coregistration of the resulting images onto MRI (substraction ictal SPECT coregistration MRI - SISCOM) has shown to increase the accuracy of this method.

References
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