Advances in neuroimaging in patients with epilepsy

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Intractable seizures can have a devastating effect on the development of a child. In children with intractable epilepsy that is refractory to medication, surgical treatment may be needed. Magnetic resonance imaging is an essential neuroimaging tool to assist in the identification of an epileptogenic substrate. The interpretation of MR images should be done in the context of clinical knowledge of the seizure symptomatology and electroencephalographic findings. Quantitative processing of structural MR data and advanced MR imaging such as diffusion tensor imaging and MR spectroscopy have the potential to identify subtle lesions that may otherwise have been missed. In addition to lesion localization, identification of eloquent cortex and white matter tracts are also an essential component of epilepsy surgery workup. Functional MR imaging maps the sensorimotor cortex and also lateralizes language. Diffusion tensor imaging tractography can be used to map the corticospinal tracts and the optic radiations. In addition to MR imaging, magnetoencephalography and nuclear medicine studies such as PET and SPECT scanning may be used to lateralize seizure focus when clinical, electrophysiological, and structural MR imaging findings are discordant. (DOI: 10.3171/FOC/2008/259/E3)

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EPILEPSY is a chronic neurological disorder characterized by spontaneous recurrent seizures, which are caused by excessive and abnormal electrical discharges from the cortical neurons. Intractable epilepsy has a devastating effect on the development of a child. Seizures may also induce brain injury. Serial MR images obtained in patients with TLE over a period of ~3.5 years have demonstrated a reduction in hippocampal volume by ~10%. In a prospective study of 122 patients with chronic epilepsy and 68 patients with newly diagnosed seizures, significant atrophy of the hippocampus, cerebellum, or neocortex has been found in 9% of newly diagnosed patients with epilepsy and in 17% of those with chronic epilepsy compared to controls. In ~30% of those with partial seizures, the disease is resistant to antiepileptic drugs. In some of these patients with intractable epilepsy, resection of the brain region that is provoking seizures may be the only effective treatment. Magnetic resonance imaging is a crucial component of the presurgical workup in children with intractable epilepsy to identify the epileptogenic substrate. In children with newly diagnosed epilepsy, MR imaging detected structural abnormality in 13% of cases. However, in patients with intractable epilepsy, the overall sensitivity of MR imaging in identifying epileptogenic substrates varies from 82 to 86%. Whereas the range of pathological substrates responsible for intractable partial epilepsy in children is similar to that in adults, cortical malformations (FCD in particular) are more commonly detected in surgical specimens obtained in pediatric patients with epilepsy. Malformations of cortical development constitute 10–50% of pediatric epilepsy cases being evaluated for surgery and 4–25% of adult cases of intractable epilepsy. Wolf and Wiestler reported a frequency of 18% for cortical dysplasia in surgical specimens obtained in a series of 216 adult patients with intractable epilepsy. In contrast, in pediatric patients with refractory epilepsy who had undergone resection, Jay et al. reported a 30% frequency of FCD, whereas Farrell et al. reported a 39% frequency of FCD. In contrast, hippocampal sclerosis is less common in pediatric patients compared to adults with intractable epilepsy. In a series of 126 children undergoing temporal lobectomy for intractable epilepsy, Benifla et al. reported that the prevalence of hippocampal sclerosis was 13%. Mittal et al. reported a higher prevalence of mesial temporal sclerosis in their cohort; of the 109 children who underwent temporal lobectomy, 45% had mesial temporal sclerosis. In contrast, hippocampal sclerosis is the most common epileptogenic substrate seen in adults with TLE.

Abbreviations used in this paper: BOLD = blood oxygen level-dependent; CBF = cerebral blood flow; Cho = choline; DT = diffusion tensor; EEG = electroencephalographic; FA = fractional anisotropy; FCD = focal cortical dysplasia; FDG–PET = [18F]fluorodeoxyglucose-PET; fMR = functional MR; FMZ = [11C]flumazenil; MEG = magnetoencephalography; MTLE = mesial temporal lobe epilepsy; NAA = N-acetylaspartate.

Structural MR Imaging

In the clinical setting, structural MR imaging remains the fundamental neuroimaging technique for identifying a lesion that could be responsible for the epilepsy. Iden-
Identification of the epileptogenic substrate on MR imaging has implications for the postsurgical outcome. The sensitivity of MR imaging for detecting a structural abnormality depends on 3 factors: 1) the pathological substrate; 2) the MR imaging techniques applied; and 3) the experience of the interpreting physician. An optimal MR technique for assessing the pathological substrate should include a variety of imaging sequences, including T1- and T2-weighted, proton density, and FLAIR sequences. These sequences need to be acquired in at least 2 orthogonal planes covering the whole brain, using the minimum slice thickness. In patients with TLE, the coronal plane should be perpendicular to the long axis of the hippocampus to optimize visualization of the hippocampus and mesial temporal lobe structures. A 3D T1-weighted volume sequence with slice thickness of ≤1.5 mm should be included because this sequence provides excellent gray/white matter contrast and can be reformatted into any orthogonal or nonorthogonal planes. The 3D volumetric T1-weighted images can also be subjected to additional postprocessing without the penalty of additional imaging time.

Current MR imaging techniques provide images with high spatial resolution, excellent soft-tissue contrast, multiplanar imaging capability, and lack of ionizing radiation. Despite improvements in the technical aspects of image acquisition, visual assessment of MR images should be done by neuroimaging experts who are knowledgeable in the field of epilepsy imaging, so as to maximize lesion detection. The interpretation of MR images should be done in the context of clinical knowledge of the seizure semiology and EEG findings.

Additional Postprocessing of Structural MR Imaging: Curvilinear Reformat

Conventional MR imaging is limited by the elaborate and irregular gyral structure, which may lead to the impression of cortical thickening and result in uncertainty and artifactual false-positive results. High-resolution MR imaging along with multiplanar reformatting improve the detection of FCD. Despite these improvements, minor structural abnormalities may still be missed on MR images. The inherent complexity of the brain’s convolutional pattern imposes limitations on the identification of subtle cortical lesions. When reconstruction of the 3D data set is performed in the orthogonal planes, the plane of analysis may be oblique to some gyri, thereby leading to apparent gyral thickening and hence a false-positive diagnosis of cortical malformation. The curvilinear reformat avoids the problem of artifactual cortical thickening because the curvilinear line is drawn parallel to the surface of the brain and therefore perpendicular to the gyri, thereby demonstrating a more homogeneous distribution of the gray matter.

Curvilinear reconstructions performed using the 3D data sets have been found to be useful to clarify the nature of suspect areas detected on conventional slices. Bastos and colleagues have also found the addition of curvilinear reconstruction to be useful in detecting subtle cortical lesions that could be missed by conventional examination. Montenegro et al. have demonstrated improved visualization of lesion location and extent by adding curvilinear reformatting to standard MR and multiplanar reformatting (Fig. 1). Further improvements have been made in the manual method of curvilinear reconstruction, by using an automated data-driven curvilinear reconstruction program.

Quantitative MR Imaging

In some patients with intractable focal epilepsy, structural MR imaging does not demonstrate a lesion. When these “MR-negative” patients underwent surgery, the outcome was found to be worse than when a lesion was detected. Histological examinations of surgical specimens obtained in these MR-negative patients have shown subtle malformations of cortical development such as microdysgenesis or gliosis. These MR images may be read as negative because a subtle lesion may not be readily detectable by qualitative assessment of the structural MR imaging. The problem with detecting some of these subtle malformations is compounded by the inherent complexity of the
brain’s convolutional pattern, which makes visual identification of these lesions difficult. Quantitative image analysis of structural MR, usually of 3D T1-weighted images, offers an objective means of analyzing MR images and therefore improves the likelihood of detecting subtle lesions. There are several quantitative methods of assessing the cortex. One method is by classifying tissues into categories such as gray matter, white matter, and cerebrospinal fluid, and then segmenting various structures by using manual or automated segmentation techniques, such as artificial neural networks,140 and 3D model-based segmentation techniques.1,57,116,129 Using this method, volumetric neocortical measurements may provide an objective way to evaluate the extent of resection and its relation to surgical results.68 Another method is voxel-based morphometry, which involves a voxelwise comparison of the local “concentration” of signal intensity between 2 groups.5 Voxel-based morphometry has been used to demonstrate neocortical gray matter reduction, either lateralized or not to the epileptic focus, demonstrating abnormalities beyond the visualized lesions.58,105,133 Texture analysis of the 3D T1-weighted images performed using voxelwise operators has been used to assess FCD. Voxelwise operators have been used to model gray matter thickness, to quantify the gray matter–white matter interface to detect its blurring, and to model hyperintense T1-weighted signals within gray matter through intensity measurement of a voxel relative to the threshold intensity between gray and white matter.2,3

Diffusion Tensor Imaging

Diffusion of water is based on the principle that the thermal energy within water molecules results in their random motion, also known as Brownian motion. In the human brain, water diffusion is restricted by macromolecules, membrane, and myelin. In the white matter, diffusion is greatest parallel to the white matter tracts but minimal perpendicular to them. This gives rise to the concept of asymmetry of diffusion of water molecules in 3 dimensions, also known as anisotropy.8 Diffusion tensor imaging allows the quantification of diffusion of water molecules and also characterizes the degree and direction of anisotropy.97 Diffusion tensor imaging is a mathematical model of an ellipsoid, and from this the 3 eigenvectors representing the principal directions of diffusion and 3 eigenvalues representing the magnitude of diffusion along these directions can be calculated. A number of diffusion parameters can be derived in each voxel.97 The mean diffusivity provides an overall evaluation of the magnitude of diffusion motion in a voxel or region.96 To measure mean diffusivity, units of square millimeters per second are used. The value for FA represents the ratio of the anisotropic component of the DT to the whole DT.10,11,97 The FA metrics are scalar indices and are unitless, and FA values range from 0 to 1, where 0 represents maximal isotropic diffusion as in a perfect sphere, and 1 represents maximal anisotropic diffusion. Most acquired insults and malformations of cortical development lead to disruption of the microstructural environment, resulting in reduced anisotropy and also a reduction in cell density and/or expansion of the extracellular space, thereby resulting in an increase in mean diffusivity.

Diffusion tensor imaging has been used to evaluate patients with malformations of cortical development and acquired lesions.108,131,132 Reduced FA and increased mean diffusivity have been demonstrated adjacent to malformations of cortical development visible on MR imaging.35,129 Increased perpendicular diffusivities have also been found adjacent to malformations of cortical development, suggesting a dominant effect of abnormal myelin in the white matter adjacent to these malformations.129 Electroencephalographic abnormalities usually extend beyond the margins of FCD that are visible on MR imaging. To improve surgical outcome, it is essential to resect these areas that demonstrate EEG abnormalities but normal results on MR imaging.121 In addition, areas of increased diffusivity and reduced FA have also been detected beyond the margins of malformations of cortical development visible on MR imaging.35 Dumas de la Roque et al. have also found reduced FA 2–3 cm distant from MR imaging–visible malformations of cortical development. This suggested that DT imaging could detect abnormalities beyond the MR imaging–visible lesion. Intercital DT imaging has the potential to identify focal abnormalities in patients with partial epilepsy and normal structural MR imaging findings. Rugg-Gunn et al. found increased diffusivity in 8 patients and reduced FA in 2 of 30 patients with refractory partial epilepsy. The areas of abnormal diffusion were thought to be caused by disruption of the microstructure due to occult dysgenesis, or by acquired damage, or secondary to repeated seizures resulting in neuronal loss, gliosis, and expansion of the extracellular space. In patients with focal epilepsy and normal structural MR findings, the areas that demonstrate diffusion abnormalities have demonstrated good spatial concordance with epileptiform activity on stereo-EEG recordings in nearly 50% of patients.41,125

Proponents of this imaging modality believe that DT imaging is superior to conventional MR imaging of the brain in its ability to determine the completeness of resection. Many authors also believe that it is superior to conventional MR imaging in determining whether the resection includes the hemorrhage or scar of gliosis associated with the area of the seizure focus, which is a critical factor in evaluating the completeness of resection.44,125 DT imaging provides 2 types of information: information about the primary area of the seizure focus and the completeness of resection of that area and information regarding other functional areas of the brain beyond the primary area that may be involved in the patient’s seizure and that must be resected to achieve a successful surgical outcome.

The goal of presurgical planning is to identify eloquent cortical areas outside the extent of the primary area of the seizure focus, which directly contribute to the generation of the seizures, and to identify other areas that may be involved in the genesis of the seizures, but that are not directly responsible for the generation of the seizures.3,126,129 Diffusion tensor imaging tracts can be acquired using the directional information obtained within each voxel to generate virtual 3D maps of white matter. Tractography allows assessment of specific white matter pathways. Both qualitative and quantitative information such as fiber density index, FA, and volume of specific white matter tracts can be obtained. Tractography can be used to evaluate the location of eloquent white matter tracts such as optic radiations and corticospinal tracts and their relation to lesions.

Due to the variability of the anterior extent of the Meyer loop, there is a risk of visual field defects following anterior temporal lobe resection. Disruption of the Meyer loop as assessed on pre- and postoperative tractography corresponded with the findings of homonymous hemianopia on visual field assessment. Preoperative and postoperative tractography of the optic radiations have also been used to predict the magnitude of pre- and postoperative visual field loss from the geometrical relationship between optic radiations and arteriovenous malformations.

Other eloquent white matter tracts that are of interest for presurgical planning include the corticospinal tracts (Fig. 2). Diffusion tensor imaging tractography has also been used to assess the white matter tracts associated with the limbic system as well as the hippocampus ipsilateral and contralateral to the seizure focus in TLE. The significance of the contralateral changes is unclear and there is as yet no consensus as to whether these changes are reversible. Thivard et al. have found that diffusion abnor-
malalties in the contralateral hippocampus were reversed following surgery in 24 patients, and suggested that the diffusion changes may represent a functional mechanism linked to the active epileptic process. In contrast, Concha et al. have found that diffusion changes in the fornix, cingulum, and external capsule in 8 patients persisted following epilepsy surgery, suggesting that the changes are secondary to structural abnormalities rather than functional changes.

Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy is a powerful adjunct to MR imaging due to its ability to probe the biochemical environment of the brain. The most commonly used nucleus is proton MR spectroscopy, which offers the ability to assess a variety of metabolites such as NAA, Cho, creatine, lactate, glutamine, and glutamate. The NAA groups are largely confined to neurons and neuronal processes and reflect the quantity and function of the bodies, axons, dendrites, and synapses of neurons. Therefore, NAA is generally considered a marker for neuronal disease and is usually reduced in pathological conditions that damage neurons. Choline is a component of phosphoglyceride and is therefore a major component of cell membranes. The Cho concentration provides information primarily about membrane turnover, the degree of myelination, and cell density. Lactate is not normally shown but may be found where anaerobic metabolism is present. Glutamate concentration in gray matter reflects the glutamate concentration in glutamatergic neurons.

Abnormalities on MR spectroscopy have been used for lateralizing TLE, as demonstrated by reduced NAA and increased Cho. The MR spectroscopy findings were consistent with the histopathological characteristics of reduced neuron cell counts or neuronal dysfunction and increased glial cell numbers. Focal reduction of NAA has been detected on proton MR spectroscopy in patients with nonlesional TLE, with good correlation with EEG abnormalities and severity of cell loss. Abnormal NAA ratios have been found ipsilateral to the ictal EEG focus in patients with normal hippocampal volumes on MR imaging. Abnormal NAA ratios have also been found contralateral to the seizure focus side, which reversed in patients who became seizure free after surgery. Reduction in NAA may relate to neuronal and glial dysfunction rather than absolute neuronal cell loss. Glutamate and glutamine levels have been found to be elevated in the temporal lobe ipsilateral to the seizure onset, including in patients with negative MR imaging findings.

In extratemporal lobe epilepsy, the ability of MR spectroscopy to lateralize the epilepsy was less than it was in TLE. In a study of patients with frontal lobe epilepsy, MR spectroscopy results enabled lateralization of the seizures in 50% of cases. The MR spectroscopy modality has been used to assess focal seizures associated with malformations of cortical development. Kuzniecky et al. have found abnormal metabolites in patients with FCD, and this correlated with frequency of seizures but not with the degree of interictal EEG discharges. These authors have also found that the quantitative neuronal and glial cell count in those who underwent surgery showed no statistically significant correlation between cell loss and the abnormal metabolite ratios. Widjaja et al. and Li et al. have found normal NAA ratios in patients with polymicrogyria and gray matter heterotopia (Fig. 3). Polymicrogyria is a malformation of cortical development that occurs secondary to abnormal cortical organization, and therefore the neurons are more mature compared to those in patients with FCD, which is a malformation secondary to abnormal neuronal proliferation or differentiation. Despite the increased number of neurons in gray matter heterotopia, which is a malformation due to abnormal neuronal migration, the NAA ratio remained relatively normal rather than...
elevated. This suggested that some of the neurons in gray matter heterotopia were dysfunctional.

**Functional MR Imaging**

Functional MR imaging is used for mapping language, memory, and sensorimotor location for presurgical planning. This imaging modality is based on the observation that increased neuronal activity is associated with an increase in CBF and therefore an increase in the oxyhemoglobin/deoxyhemoglobin ratio. This is the principle of BOLD imaging that forms the basis of fMR imaging, which allows the mapping of neural networks. There are circumstances in which the BOLD response may be perturbed, resulting in unreliable findings. These include situations such as the presence of a large tumor with mass effect and edema, vascular malformations, and the postictal state.

A major role of fMR imaging in epilepsy surgery workup is in lateralizing language functions (Fig. 4) as a means to supplement or replace the intracarotid amobarbital test. Studies have demonstrated a $\approx 90\%$ concordance with the intracarotid amobarbital test. In the remaining 10% of patients who demonstrated disparity between fMR imaging results and the amobarbital test, fMR images were more likely to show bilateral language dominance compared to the other test. A panel of tasks, including verbal fluency and language comprehension, has been advocated...
to increase the reliability of fMR imaging. This modality also predicted language deficits following epilepsy surgery and could influence surgical planning.

The correlation between fMR imaging results and disruption of function associated with electrocortical stimulation has been assessed. The specificity of fMR imaging compared to electrocortical stimulation was 67%, and the sensitivity was > 90%. Activation on fMR images and disruption of function as assessed with electrocortical stimulation was within 5 mm in frontal regions and 10 mm in temporal areas. Differences in the results of fMR imaging and electrocortical stimulation may be due in part to inability of electrocortical stimulation to map areas deep within sulci, coregistration error in fMR, BOLD identification of draining veins rather than capillaries, or the threshold used for processing fMR images.

Sensory and motor tasks are the most reliable and reproducible fMR paradigms. Functional MR motor mapping has been found to have excellent agreement with intraoperative cortical mapping. It is crucial to assess memory functions prior to planning anterior temporal lobe resection. There are currently too few studies of healthy volunteers and patients to validate memory paradigms for clinical practice. Agreement between fMR imaging and intracarotid amobarbital test results has been found to be 50–60%. Further work is required to establish a battery of reliable fMR memory paradigms and a panel of memory tasks to identify the ability of the unresected side to sustain memory postoperatively and also to predict postoperative memory performance.

**Magnetoencephalography**

When combined with structural MR imaging, magnetoencephalography (also known as magnetic source imaging) is a noninvasive tool for epilepsy localization. The MEG modality measures extracranial magnetic fields perpendicular to the direction of intracellular currents in apical dendrites. Therefore, MEG measures currents flowing tangential to the scalp, corresponding to sulcal activations. One of the advantages of MEG as opposed to EEG studies is that magnetic fields are minimally affected by conductivities of intervening structures and tissues between brain and scalp. The MEG spike sources have been found to correlate with invasive monitoring in which subdural grids and intraoperative electrocorticography are used in children with intractable epilepsy. Magnetoencephalography is well suited for identifying the epileptogenic foci in the pediatric population, in which neocortical epilepsy is more common compared with MTLE. In children with normal or subtle nonfocal MR imaging results, MEG findings have been found to predict surgical outcome. In patients with recurrent seizures following unsuccessful epilepsy surgery, MEG has a role in localizing postsurgical epileptiform disturbances, because MEG is less affected by the biophysical disturbances of cranial defects and brain volume changes. One of the limitations of MEG is in identifying epileptiform paroxysms from deep-seated areas such as the mesial temporal lobe. Deep-seated sources require > 6 cm² of contiguous cortical activity, whereas lateral neocortical sources require 3–4 cm² of neocortical activity to be detected on MEG.

Another role of MEG in pediatric epilepsy is the presurgical mapping of eloquent cortex. This modality has an advantage compared to fMR imaging in mapping the eloquent cortex; MEG directly measures the electrophysiological changes underlying neuronal activity and also has higher temporal resolution compared to fMR. In contrast,
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fMR imaging relies on the detection of changes in regional CBF and volume to assess the functional activity of the brain.

**Positron Emission Tomography**

The role of interictal FDG–PET in the presurgical assessment of intractable epilepsy is to determine the lateralization of the epileptic focus. The glucose hypometabolism volume is often widespread, although ictal onset zones typically are located at the sites of the most severe hypometabolism within the larger volume. Intercital FDG–PET hypometabolism, when appropriately correlated with MR imaging findings, EEG recordings, and other clinical data, can be used to lateralize the side of seizure onset, guide placement of intracranial electrodes, and determine the prognosis for complete seizure control following surgery. Patients with refractory mesial temporal lobe seizures usually have widespread temporal lobe hypometabolism, including lateral temporal lobe and ipsilateral frontal, parietal, thalamic, or basal ganglia hypometabolism. Normal interictal metabolism also occurred in refractory MTLE, but normal FDG–PET scans were more common in nonrefractory than in refractory MTLE. Focal mesial temporal hypermetabolism sometimes occurred interictally in children with MTLE, but rarely occurred in adults with focal epilepsies. This could be attributed to continuous repetitive focal mesial temporal seizures, which were subclinical and not detectable with scalp electrodes, or to interictal epileptogenic processes that were peculiar to children. Unilateral temporal lobe hypometabolism is “false-positively localized,” that is, located contralateral to the intracranially recorded site of ictal onset, in ~ 1-2% of patients.

 Patients with neocortical localization-related epilepsies have a widespread hypometabolic region on interictal FDG–PET scans, which include areas such as the thalamus and basal ganglia ipsilateral to the neocortical site of hypometabolism. When associated with a lesion, the diffuse hypometabolic area of the neocortex is often much larger than the associated structural imaging abnormality (Fig. 5). The area of hypometabolism, excluding the site of MR imaging-visible structural lesion, usually contained the electrophysiologically defined ictal onset zone. In the absence of a structural lesion on MR imaging, the volume of diffuse regional hypometabolism sometimes may be fairly small in neocortical epilepsies. Intercital focal neocortical areas of hypermetabolism may occur in early childhood epilepsies. In neocortical epilepsies and in localization-related epilepsies that cannot be fully characterized by electroclinical manifestations, interictal FDG–PET abnormalities cannot be used to determine the margin of cortical resection, but can be used with other data to determine sites that should be monitored with intracranial electrodes.

 The absence of hypometabolism does not rule out localization-related epilepsy. Similarly, regional hypometabolism strongly suggests that seizures may begin somewhere within that region, but does not rule out multiple areas of ictal onset within and beyond the hypometabolic cortex. Intercital regional hypometabolism has been found to be useful in predicting seizure outcome following temporal lobe resection. The more severe the hypometabolism of the temporal lobe, the better the postsurgical outcome with respect to seizure control. Other more commonly used PET ligands for assessing intractable epilepsy include FMZ, which acts as a specific reversibly bound antagonist at the benzodiazepine-binding sites of the γ-aminobutyric acid receptor. On PET scans, FMZ shows as an area of reduced uptake in the epileptogenic focus. The area of reduced FMZ binding has been found to be more restricted than the area of hypometabolism on FDG–PET in TLE. The FMZ PET scan was more sensitive than MR imaging in the detection of contralateral abnormalities, which were found in one-third of patients with apparent unilateral hippocampal sclerosis on MR imaging. In patients with extratemporal lobe epilepsy, FMZ PET demonstrated reduced uptake in all 6 of those with acquired lesions and a focal increase in uptake in 10 of 18 patients with normal results on MR imaging. In patients with malformations of cortical development, a focal increase in uptake of FMZ has been reported to be more extensive than the abnormality found on MR imaging, and was also noted in distant sites that were unremarkable on MR imaging.

**Single-Photon Emission Computed Tomography**

The role of SPECT studies is to lateralize or localize the site of seizure onset when imaging is nondiagnostic and other noninvasive presurgical evaluations are unable to lateralize or identify the epileptogenic zone. The SPECT studies involve CBF imaging using radiopharmaceutical materials, principally either technetium-99m hexamethylpropyleneamine oxime or technetium-99m bicisate, which have rapid first-pass brain extraction, with maximum uptake being achieved within 30-60 seconds of an intravenous injection. The SPECT images can be acquired up to 4 hours after the injection so that the patient can recover from the ictus before undergoing imaging. The SPECT studies require a combined ictal and interictal examination. The ictal SPECT examination will identify focal hyperfusion, whereas the interictal SPECT examination will identify focal hypoperfusion in the region of the epileptogenic zone. The diagnostic yield of ictal SPECT is superior to interictal SPECT alone. The rationale for interictal SPECT imaging is to serve as a reference or baseline study for the interpretation of ictal SPECT images. Intercital SPECT on its own has low sensitivity and a high false-positive rate in TLE, and a low diagnostic yield in patients with extratemporal seizures. A potential limitation of ictal SPECT imaging is that the spatial resolution of these studies is inferior to that of PET scans. Following image acquisition, the coregistered and normalized interictal images can be subtracted from the ictal images and then coregistered onto high-resolution MR images with the aid of computer software. Such a paradigm is known as “subtraction ictal SPECT coregistered to MR imaging” (also known as SISCOM). This modality has been shown to indicate the location of the epileptogenic zone reliably, and has been found to be superior to the traditional visual analysis of the interictal and ictal images. This technique can be used successfully in pediatric patients.

**Conclusions**

Structural MR imaging remains a crucial tool in the eval-
vation of children with intractable epilepsy. Correlation and concordance of the MR imaging-identified substrate with clinical and electrophysiological data is essential to avoid false-positive localization of the epileptogenic substrate. Advanced MR imaging techniques such as DT imaging and MR spectroscopy and various quantitative analyses of structural MR images have the potential to detect subtle lesions that may be responsible for the epilepsy or to later-alyze seizure focus. Another major role of additional MR techniques such as fMR and DT imaging is to identify elo-
quent cortex and white matter tracts, respectively. The MEG, PET, and SPECT imaging modalities may also be used to lateralize seizure focus when clinical, electrophysiological, and structural MR findings are discordant.

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