NEUROIMAGING IN TSC

Neuroimaging (imaging of the brain) is one of the most important tools used in the diagnosis and management of tuberous sclerosis complex (TSC). Imaging in TSC usually involves computed tomography (CT) and/or magnetic resonance imaging (MRI) scans of the brain. Newer imaging techniques, such as positron emission tomography (PET), magnetoencephalography (MEG), and diffusion tensor imaging (DTI) have been used for detecting specific changes in the brain. The most common findings include cortical tubers, subependymal nodules, and subependymal giant cell astrocytomas (SEGAs).

After the diagnosis of TSC has been made, periodic follow-up scans may help identify areas of change or deterioration or be used for presurgical evaluation for individuals with intractable epilepsy. Each of these sophisticated tests has strengths and weaknesses. It is common for them to be used in combination (MRI plus one or more other method) during the presurgical evaluation as part of the effort to find the best area for resection (Evans et al., 2012). These techniques will be described in this Information Sheet, as well as their usefulness and limitations in individuals with TSC.

Computed Tomography
Computed Tomography (CT) scans produce a picture of the brain by directing a beam of X-rays through the targeted area at many different angles. A detector measures how much of the beam comes out on the other side. A computer then constructs a cross-sectional picture of the brain, based on many hundreds of readings from the detector. CT scans take less time to perform than MRIs. In fact, some machines can scan the brain in as little as 25 seconds. Nonetheless, it is important that a person hold as still as possible during the scan, so that the best possible pictures can be obtained.

CT scans can show tumors, but usually not as clearly as an MRI. Calcification is better seen with CT than with MRI and sometimes can be a clue to making the diagnosis in someone not already known to have TSC. (Figure A)

Build-up of fluid in or around the brain (hydrocephalus) can also be seen well on CT scans. Because they can be performed relatively quickly and are more easily available than MRIs, CT scans can help to exclude a major abnormality or dramatic change, such as tumor growth or hydrocephalus. When a person with TSC has a sudden change in behavior, increase in seizures, or the abrupt onset of severe headaches, these symptoms can sometimes indicate that there has been such a change and may warrant the need for an urgent CT scan.

Figure A: CT scan showing calcified subependymal nodules. Cortical tubers are also present, but not as well seen compared to MRI.
Disadvantages of the CT include lower resolution (shows much less detail) than MRIs and the need for exposure to radiation (albeit at very small doses).

Magnetic Resonance Imaging (MRI)
MRIs involve placing a person in a large cylinder, open on both ends, inside a very strong magnet. MRIs provide a much more detailed picture of the brain. They can also be used to identify blood flow, chemical composition, flow of spinal fluid, and blood vessels in various areas of the brain. They can identify tubers much better than CT scans, particularly when using a technique called FLAIR (fluid attenuated inversion recovery).

![MRI Image](image)

Contrast (dye) is usually given through a vein in the arm during the scan to help determine if a subependymal nodule is beginning to grow into a SEGA. An MRI is better than CT scan for assessing any changes in tubers, tumors, or subependymal nodules that can occur over time. An MRI scan does take much longer to perform than a CT scan — as long as 45 minutes to an hour — and some special scans may take even longer.

The space in the magnet for the person being scanned is rather small, and some people may get claustrophobic. So-called “open” MRIs have magnets that are open on the sides, and are less confining. However, their image quality is not as good as that from standard MRI machines, so open MRIs are not desirable for use for individuals with TSC.

It is very important to hold perfectly still during an MRI, as the pictures are easily distorted by movement. Most children and many adults will require sedation. An advantage is that an MRI does not require exposure to radiation. This advantage is important since many people with TSC need to have several brain scans over a lifetime. In fact, some patients may require brain scans multiple times a year, although most are performed every 1-2 years until adulthood. Adults typically require MRIs of their brain less frequently unless they have a known SEGA that requires continued monitoring.

Magnetic Resonance Angiography (MRA)
Magnetic resonance angiography is a screening tool that can also be obtained during an MRI scan when there is a concern about the blood vessels in the brain. Cerebrovascular occlusive disease and vascular abnormalities or aneurysms are sometimes identified in individuals with TSC. What makes these findings unique in TSC is that they are identified in individuals with TSC at much younger ages (teens and early 20s) than in the general population.
Fetal MRI

MRI may play a prominent role in the evaluation of pregnancies at risk for TSC (Curatolo and Brinchi, 1993). The brain lesions in TSC can be seen as early as 26 weeks gestation, but unfortunately, the sensitivity of MRI for these is low in the fetus and so a "negative" study cannot rule out brain involvement by TSC (Garel 2004). If a fetus has cardiac rhabdomyomas observed using fetal ultrasonography and the concomitant presence of both subependymal nodules and cortical tubers in the brain, a definitive diagnosis of TSC can be made.

Diffusion Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI)

Diffusion MRI is a magnetic resonance imaging method that produces images of the brain by measuring how water is allowed to move in the brain tissues. Diffusion weighted MRI can provide information about damage to parts of the nervous system. Diffusion tensor MRI can provide information about connections among brain regions. DWI and DTI (Figure 2) may be useful in TSC to identify abnormal brain regions in the presurgical evaluation for epilepsy surgery.

Figure 2: DTI image of brain pathways.
Positron Emission Tomography

Positron emission tomography (PET) is a non-invasive imaging tool that measures the regional uptake and use of substances by the brain and other organs. (Figure 3) For the brain, PET has been used to identify the specific area or areas causing seizures in presurgical evaluations for epilepsy surgery and to study cognitive aspects of various disease conditions, including TSC. PET has two major roles in epilepsy surgery for TSC: 1) to detect cortical tubers as well as surrounding dysplastic (abnormal) areas with high sensitivity; and 2) to assess the full extent of functional abnormality in the opposite side of the brain, thereby predicting the possible impact of surgery on cognition.

Figure 3: PET (picture on left) correlated with MRI (picture on right).

Magnetoencephalography

An improvement in functional localization of the seizure focus can be obtained by combining electroencephalogram (EEG) and magnetoencephalography (MEG) signals. MEG measures magnetic fields that are primarily associated with intracranial (brain) currents. MEG is better than EEG in the ability to pick up the currents in the brain and thus may better localize the source of the seizures.

Magnetic source imaging (MSI) combines MEG data on brain function with MRI data on brain structure. MSI allows for more accurate localization of the area that is abnormal and the source of the seizures. It remains unclear to what extent MSI will be of assistance in avoiding invasive studies in surgery candidates and in helping the neurosurgeon to perform individualized and conservative brain resection in individuals with intractable focal seizures.
associated with TSC. However, recent studies show promising results utilizing MSI for individuals with TSC (Iida et al., 2005; Janssen et al., 2006; Wu et al., 2006; Carlson et al., 2011).

![Magnetoencephalography fused with MRI image](image)

**Figure 4: Magnetoencephalography fused with MRI image**

**Single-Photon Emission Computer Tomography (SPECT)**

A SPECT scan is a type of nuclear imaging test, which means it uses a radioactive substance and a special camera to create 3-D pictures. The test may be done either during a seizure (ictal), or in between seizures (interictal) to determine blood flow to areas where the seizures starts. A radioactive substance is given through an intravenous (IV) infusion into a vein in the arm. The tracer’s radiation dose is very small; the amount of radiation exposure is less than that of a chest X-ray or CT scan. During the scan, the patient lies on a table while the SPECT machine rotates around the head. The injected radioactive tracer is eliminated from the body by the kidneys over the next 1-2 days.
Sedation

Many people will need to be sedated during imaging studies. It is critical that sedation be performed safely and by experienced personnel. It should be sufficient to keep the individual asleep throughout the entire procedure. Taking mild sedatives prescribed by a family doctor are almost always inadequate. In fact, many people become more anxious or agitated when they receive such a medicine. Since CT scans without contrast can be done quickly, sedation is often not necessary. Scheduling a scan when a child is already sleepy or just after an infant has been fed (“milk sedation”) can be very useful.

For MRI scans, infants and young children are often sedated with an oral medicine. Older children usually need intravenous sedation. Certain people may require an anesthesiologist to be safely and adequately sedated. Whichever technique is used, it is important to be sure staff members at the imaging facility are thoroughly trained and able to handle any problems that may arise. This is particularly true for infants and children and for severely affected adults with TSC. The risk of complication from sedation for these imaging tests is far less than 0.1%.

References


