

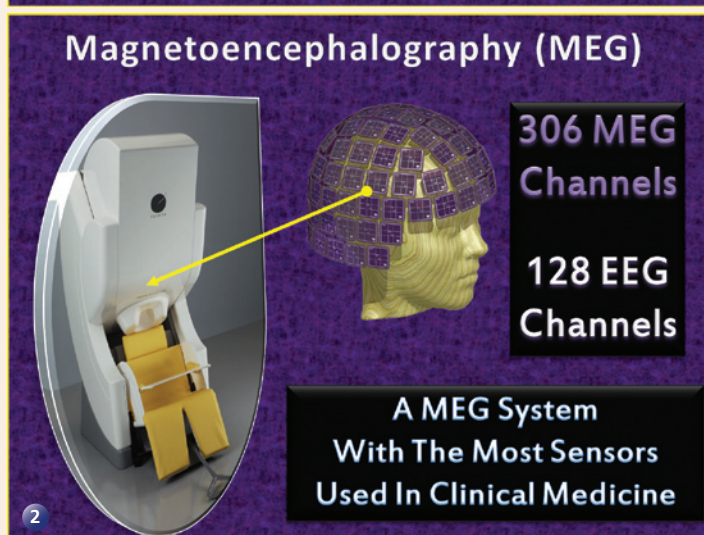
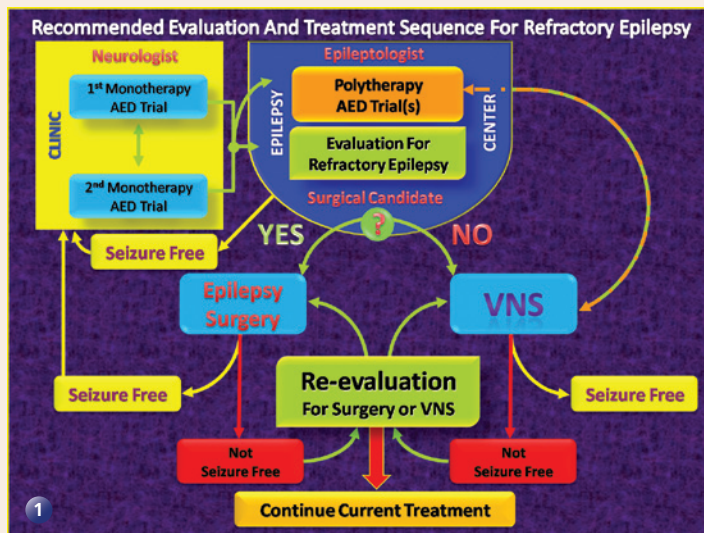
A closer look at presurgical evaluation of patients with epilepsy

by Anto Bagic, MD

While epilepsy fascinated humanity for millennia, it appears that over the last 4000 years—as a society and profession—we had only managed to replace ignorance with some knowledge while superstition and stigma towards persons with epilepsy (PWE) unfortunately persisted. Regrettably, having four times more antiepileptic drugs (AEDs) did not change the fact that one third of all treated epilepsy patients continue to seize in spite of our best efforts. Furthermore, best estimates suggest that in spite of Class I evidence and proactive clinical practice guidelines we offer the only potential cure—epilepsy surgery—to only one in 30 patients who could greatly benefit from it. There is no comprehensive research to explain this phenomenon, but an informed practitioner could suspect several elements: some physicians' reservations about brain surgery, some physicians' low level of comfort with referring for surgery, public fears regarding brain surgery, widespread misconceptions about surgical interventions, etc. Presumably a mixture of these factors is in the background of difficulties that the ROSE trial ([www.epilepsysurgery-rosetrial.com/\(412\)683-7279](http://www.epilepsysurgery-rosetrial.com/(412)683-7279)) has had in recruiting patients with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). This randomized controlled trial is aimed at comparing classical surgery and radiosurgery as treatments for this surgically remediable epilepsy syndrome.

In spite of sustained efforts of the ILAE on defining medically refractory epilepsy as “failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom,” it is still not rare to have a patient referred for a specialty evaluation to the Comprehensive Epilepsy Center on three AEDs none of which is titrated sufficiently. While it was established over five years ago that a failure of two AEDs leaves only a 2% chance that trying the next four would control seizures, even many epileptologists continue to cycle through all AEDs available before referring PWEs for further evaluation and thus directly contribute to an almost 20-year-long delay in referring for non-pharmacologic treatments of PWEs including potentially curative surgery.

Currently, upon experiencing their initial seizures, patients invariably have an EEG and brain MRI with epilepsy protocol. Usually, nothing else is necessary for an adequate pharmacologic treatment of adult patients at diagnosis. Persons failing two AEDs given long enough at appropriately titrated doses should be referred to an epilepsy center for an evaluation for intractable epilepsy. Here (figure 1) the patient may need to complete an EEG and MRI evaluation if they are inadequate for any reason or uninformative and be referred for electro-clinical correlation of their spells using a V-EEG (video-EEG) in the Epilepsy Monitoring Unit (EMU), where their medications are tapered or weaned (as appropriate and necessary) in order to increase the monitoring yield by documenting enough habitual events of interest. It is inappropriate and not medically indicated to refer a patient for any other neurological studies for their suspected epileptic spells before they undergo a complete V-EEG and their events are confirmed to be epileptic. While in the EMU, the patients also have neuropsychological testing that is not only a cross section of their cognitive performance but also has a role in helping seizure localization; a pre-WADA procedure may be performed in patients who are having their epileptic focus in dominant hemisphere. For patients with remaining ambiguities in localizing the



epileptic focus, a SPECT injection may have to be performed. Once a sufficient number of habitual events of interest is documented (this may mean more than five events for those with bilateral seizure onset or multiple types of events) the patient may be referred for additional non-invasive studies to assist seizure localization in ambiguous cases: a PET study and magnetoencephalography (MEG) to provide non-redundant localizing information that are not supplied by non-invasive EEG-based studies.

The value of MEG (figure 2) in selected cases has been established and supported by ample literature. A MEG is the most powerful method for studying brain function directly non-invasively based on the magnetic fields generated by the neural currents underlying normal and pathological brain functions as reflected outside the skull. UPMC is among 20 selected premier institutions in the country that have had the most advanced MEG-EEG system in operation for more than five years. By appropriately combining expertly and comprehensively interpreted MEG-EEG with traditional methods of presurgical evaluation (EEG, V-EEG, MRI, SPECT, PET, and WADA), the University of Pittsburgh Comprehensive Epilepsy Center's teams (adult housed in the UPMC Presbyterian and pediatric stationed in Children's Hospital of Pittsburgh of UPMC) succeed in deeming many traditional “non-surgical candidates” seizure-free. •