FIG. 1. Schematic diagram of the International Classification of Epilepsies and Epileptic Syndromes.

Nguyen The Tich S, Pereon Y. Epilepsia 1999;40:531

EME: Early Myoclonic Encephalopathy
EIEE: Early Infantile Epileptic Encephalopathy
BNFC: Benign Neonatal Familial Convulsions
BNC: Benign Neonatal Convulsions
BMEI: Benign Myoclonic Epilepsy in Infancy
Neuroimaging over the course of a patient’s epilepsy

Newly Diagnosed Epilepsy → Treatment-resistant Epilepsy → Pre-surgical Evaluation
Before Imaging - Localization

- John Hughlings Jackson (1820 – 1903)
  - Correlated seizure symptoms with anatomic location of cerebral lesions
  - “Jacksonian March” seizure
    - Motor seizure propagating along 1° motor cortex
Before Imaging - Surgery

• William Macewen (1848 – 1924)
  – Correctly localized a frontal meningioma based on “Jacksonian March” seizures
  – Tumor removed in 1879
  – Patient survived and was seizure free
History – Imaging

- 1904 – skull X-rays
- 1919 – pneumoencephalography
- 1927 – cerebral angiography
- 1971 – CT
- 1977 – MRI
The first publication of skull radiographs in diagnosing tumor in Transactions of the American Röntgen Ray Society in 1904


©2000 by Radiological Society of North America
Normal lateral pneumoencephalogram

Lateral common carotid arteriogram of GBM obtained during the early phase

Transverse CT scan obtained after the administration of contrast material depicts a large ring lesion (arrow) in the left frontal corticomedullary junction.
Emergent neuroimaging - CT indicated in a child of any age with a postictal focal deficit (Todd’s paresis) not quickly resolving, or who has not returned to baseline within several hours after a seizure.

* Neurology 2000; 55:616-623
Who needs a CT in the ED?

• 500 children with 1\textsuperscript{st} non-febrile sz
  – 475 imaged in the ED
  – 8\% with “clinically significant” abnormalities
  – 3/475 had findings needed immediate intervention
    • 1 shunt failure
    • 1 increased intra-cranial pressure after head trauma
    • 1 with new-onset infantile spasms and a neoplasm

Who needs a CT in the ED?

- High-risk groups to image in the ED
  - Known bleeding or clotting disorders
  - Known hx of malignancy
  - HIV infection
  - Closed head injury
  - Less than 33 months with a focal seizure

Newly Diagnosed Epilepsy

**Non-emergent neuroimaging** - To detect abnormalities that may affect prognosis and therefore have an impact on long-term treatment, management (*or genetic counseling*). **MRI** should be seriously considered in any child with:

- Serious cognitive or motor impairment of unknown etiology
- Unexplained abnormalities on neurologic examination
- Focal onset seizures
- EEG abnormality not primary generalized or (benign) focal

* Neurology 2000; 55:616-623
Indications for Structural Neuroimaging *

- Focal epilepsy
- Abnormal neurological exam
- Developmental delay or regression
- Symptomatic generalized epilepsy (e.g. LGS)
- Worsening seizures
- Children < 2 years
- New onset seizures and acute medical emergency

* Could it be a tumor?  
* ILAE Subcommittee for Pediatric Neuroimaging
Epilepsia, 2010
Seizures and brain tumors

- 200 consecutive children with new diagnosis of brain tumor
  - 30/200 (9%) presented with a seizure
  - 19/30 had focal seizures
  - 11/30 had generalized seizures

Wilne et al. AJDC 2006;91:502-506
Seizures and brain tumors

• 30 patients presenting with seizures
  – 17 had no other symptoms and a normal exam
    • 14/17 focal seizures
    • 3/17 generalized seizures
      – 2/3 had focal slowing on EEG
      – 1/3 atypical absence seizures

Wilne et al. AJDC 2006;91:502-506
Disorders Where Imaging May be Unnecessary

- Primary generalized epilepsies
  - CAE
  - JME
  - GTCs on awakening
- Genetic or presumed genetic focal epilepsies
  - Rolandic epilepsy of childhood
  - Occipital epilepsy of childhood
- Simple febrile seizure

* ILAE Subcommittee for Pediatric Neuroimaging
  Epilepsia, 2010
Recommended Anatomic MRI Epilepsy Protocol at 1.5 Tesla *

- Thin-slice volumetric T1WI - gradient echo**
- T2WI - spin echo: FSE or dual echo (axial, coronal)
  - High sensitivity for most brain lesions
  - Gradient echo if hemorrhagic lesion, calcification suspected
- Flow attenuation inversion recovery (FLAIR) T2WI: cancel water, improve contrast
- High resolution oblique coronal T2WI- fast or turbo spin echo
- Maximal slice thickness < 4-5 mm

* ILAE Subcommittee for Pediatric Neuroimaging Epilepsia, 2010
** must include sagittal plane to detect midline abnormalities
Newly Diagnosed Epilepsy

FLAIR
New-onset Afebrile Seizures in Infants*

- Prospective evaluation of 319 infants
  - CT- 94%
  - MRI- 57%
- One-third of CT scans-abnormal; 9% required acute medical management
- One-half of MRIs abnormal; half had MCDs

* Hsieh et al, Neurology; 2010
major cerebral malformations

hemimegalencephaly  polymicrogyria  schizencephaly  hemidysplasia

meningeal angiomatosis  tuberous sclerosis  diffuse heterotopia  agyria / pachygyria
MRI detection of focal cortical dysplasia at 1.5 T

Newly Diagnosed Epilepsy
focal epileptogenic lesions

- hippocampal sclerosis
- dysembryoplastic NET
- ganglioglioma
- hypothalamic hamartoma
- focal cortical dysplasia
- encephalomalacia

Newly Diagnosed Epilepsy
Recommended Anatomic MRI Epilepsy Protocol at 1.5 Tesla

Special Considerations

- GAD: reserved for suspected tumors, vascular malformations, inflammatory disorders
- Sedation: typically required for children < 7 yrs
- MRS: for suspected metabolic disorders
- Infants: Immature myelination under 2 years
  - Axial, coronal and sagittal T1WI
  - High resolution T2WI

* ILAE Subcommittee for Pediatric Neuroimaging Epilepsia, 2010
Imaging and outcome prediction in a population-based study

- **127** children with new-onset epilepsy before 36 months followed for a median of 78 months
- 35% had treatment-resistant seizures
- Significant predictors on multivariate analysis:
  - Age ≤12 months at diagnosis (OR 6.76, 95% CI 2.00, 22.84, p=0.002)
  - Developmental delay at initial diagnosis of epilepsy (OR 20.03, 95% CI 3.49, 114.83, p=0.0008)
  - Neuroimaging abnormality (OR 6.48, 95% CI 1.96, 21.40, p=0.002)
  - Focal slowing on initial EEG (OR 5.33, 95% CI 1.14, 24.88, p=0.03)

*Wirrell et al. Epilepsia 2012;53:1563-9*
Neuroimaging and evolution of epilepsy

- Newly Diagnosed Epilepsy
- Treatment-resistant Epilepsy
- Pre-surgical Evaluation
Population of children who are treatment-resistant and MRI-negative ("non-lesional")

GOAL - Identification of subtle focal abnormality

May require advanced imaging modalities:

- High field strength magnet (3T, 4T)
- Other MR sequences
- MEG
- PET, Ictal SPECT
Increased detection and differentiation of previously missed focal cortical lesions:

- 64% - Grant et al, 1997
- 37.5% - Knake et al, 2005
- 20% - Strandberg et al, 2008

Change in magnet strength requires new determination of range of normal
MEG: Interictal sharp waves with non-lesional MRI
Neuroimaging and evolution of epilepsy

Newly Diagnosed Epilepsy → Treatment-resistant Epilepsy → Pre-surgical Evaluation
Goals of the Pre-surgical Evaluation:

- Localize the Epileptogenic Region (ER)
- Define relationship of the ER to Critical Cortex (CC)
- Resection = ER - CC
Neuroimaging in the Preoperative Evaluation for Pediatric Epilepsy Surgery

- Anatomically define extent of the lesion (MRI-positive) and the epileptogenic zone (MRI-negative)
- Anatomically define regions of cortical eloquence
- Define the relationship between the lesion, epileptogenic zone and eloquent cortical lesion (Surgical Plan)
Neuroimaging in the Preoperative Evaluation for Pediatric Epilepsy Surgery

- Functional neuroimaging
  - fMRI
  - MEG
  - PET, SPECT

- Image co-registration
Focal cortical dysplasia – discordant data (SGE)
Tuberous Sclerosis – multiple cortical tubers

MRI

Ictal HMPAO SPECT
Pre-surgical Evaluation

Functional MRI - language (dysplasia)
MEG: Also for functional testing

Co-register as many modalities as possible

Intra-operative testing if needed
Newly Diagnosed Epilepsy

Practice parameter: Evaluating a first non-febrile seizure in children: Report of the Quality Standards Committee of the AAN, CNS and the AES

**Emergent neuroimaging** - CT indicated in a child of any age with a postictal focal deficit (Todd’s paresis) not quickly resolving, or who has not returned to baseline within several hours after a seizure.

**Non-emergent neuroimaging** - To detect abnormalities that may affect prognosis and therefore have an impact on long-term treatment, management, *or genetic counseling*. MRI should be seriously considered in any child with:
- a serious cognitive or motor impairment of unknown etiology
- Unexplained abnormalities on neurologic examination
- Seizure of focal onset
- EEG abnormality not primary generalized or (benign) focal

* Neurology 2000; 55:616-623
Case

• Focal clonic seizure of the right arm at 4 months
  – Lasted 15 minutes
  – Post-ictal Todd’s paralysis on right

• GTC at 5 months
  – Lasted 30 minutes

• Exam and development normal

• MRI
  – Abnormal signal in left posterior frontal - parietal region

• Myoclonic seizures by 12 months
Case

- **Inter-ictal EEG**
  - L and R focal sharp waves, and generalized spike and wave
- **Ictal recording at 14 months**
  - GTCs and myoclonic seizures
  - Irregularly generalized spike and wave at ictal onset, some with L predominance
- **Intra-cranial EEG at 18 months**
  - L frontal and parietal grids, including L inter-hemispheric strips
  - GTC – L parietal inter-hemispheric onset
  - Myoclonic – generalized spike and wave
Case

- L mesial parietal resection
- Pathology
  - Limited specimen
  - No dysplasia, no gliosis
- Seizures persist
Case

• SCN1A DNA sequencing test
  – Frame shift mutation (insertion) leading to premature stop codon
  – Parents do not carry the mutation

• Imaging is always just part of the story