American Society of Neuroimaging

Neuroimaging in Epilepsy

January 15, 2016 • Orlando, Florida

Joshua P. Klein, M.D., Ph.D.
Chief, Division of Hospital Neurology
Associate Professor of Neurology and Radiology
Brigham and Women’s Hospital & Harvard Medical School
Background

MRIs read by radiologists outside of epilepsy centers failed to detect 50% of focal epileptogenic lesions.

Risks for missing lesions:
- Perceptual misses due to limited knowledge of seizure-producing lesions
- Incomplete knowledge of patient history
- Poor judgment
- Poor technique
Table 1  
Response to **medical treatment** as a function of syndrome and lesion in chronic focal epilepsy [1].

<table>
<thead>
<tr>
<th>Syndrome and etiology</th>
<th>Seizure control (&gt;1 year seizure free) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptogenic focal epilepsy</td>
<td>45</td>
</tr>
<tr>
<td>Symptomatic focal epilepsy</td>
<td>35</td>
</tr>
<tr>
<td>Temporal lobe epilepsy</td>
<td>20</td>
</tr>
<tr>
<td>TLE with HS</td>
<td>11</td>
</tr>
<tr>
<td>TLE without HS</td>
<td>31</td>
</tr>
<tr>
<td>Dual pathology (HS+)</td>
<td>3</td>
</tr>
<tr>
<td>Extratemporal focal epilepsy</td>
<td>36</td>
</tr>
<tr>
<td>Cerebral dysgenesis</td>
<td>24</td>
</tr>
</tbody>
</table>

TLE = temporal lobe epilepsy; HS = hippocampal sclerosis
Background

Nearly one-third of patients with focal epilepsy become refractory to medications.

In patients with refractory epilepsy…

*MRI detected 83% of causative lesions*

*CT detected 58% of causative lesions*

‘Standard’ MRI inadequate for evaluation of patients with refractory epilepsy

Radiology 1986;160(1):215
JNNP 2002;73:643
Background

In patients with unilateral medial temporal lobe epilepsy or tumors, resection yields seizure freedom in 60-80% of cases.

...malformations of cortical development, resection yields seizure freedom in 40-70% of cases.
Objectives

1) Lesion detection: the right technique and the proper clinical context

2) The imaging appearance of typical epilepsy-associated lesions
What are the indications for neuroimaging?

Evidence of focal or multifocal onset of seizures by history or EEG

Unclassified or generalized seizures in early life or in adulthood

Focal fixed neurological deficit or regression

Evidence of a neurocutaneous syndrome

Difficulty controlling seizures with first-line AEDs

Changes in seizure semiology
What are we looking for?

- Malformations of cortical development (dysplasias)
- Mesial temporal / hippocampal sclerosis
- Tumors
- Vascular malformations and anomalies
- Infarctions or hemorrhages
- Traumatic brain injury
- Infections (encephalitis, abscess, meningitis, granulomas, cysts)
<table>
<thead>
<tr>
<th>Sequence</th>
<th>Utility</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1, 1-1.5mm</td>
<td>focal cortical dysplasias</td>
</tr>
<tr>
<td>T2, 1-1.5mm</td>
<td>focal cortical dysplasias</td>
</tr>
<tr>
<td>Coronal oblique</td>
<td>temporal lobe pathologies</td>
</tr>
<tr>
<td>GRE or SWI</td>
<td>hemosiderin &amp; calcification</td>
</tr>
<tr>
<td>T1 post-contrast</td>
<td>masses &amp; vascular lesions</td>
</tr>
</tbody>
</table>
Coronal oblique

A

Sylvian fissure

B
Cavernous malformation
52F with focal seizures

T2-FLAIR

T2-FLAIR

GRE
52F with focal seizures

T2-FLAIR

T2-FLAIR

GRE

Developmental venous anomaly (DVA)
Normal cortical development

- aRGC: Apical (VZ) radial glial cell
- bRGC: Basal (SVZ) radial glial cell
- CP: Cortical plate
- IPC: Intermediate progenitor cell
- MZ: Marginal zone
- NPC: Neuroepithelial progenitor cell
- SP: Subplate
- SVZ: Subventricular zone
- VZ: Ventricular zone

Order of birthdate and lamination:
- L1
- L2
- L3
- L4
- L5
- L6

Intracerebral projections
Subcerebral projections

Gliogenesis

TRENDS in Genetics 2015;21(2):77
During myelination, white matter becomes T1 hyperintense and T2 hypointense.
Cortical migrational disorders

Gray matter heterotopia

Ellison and Love. Neuropathology 2004
Cortical migrational disorders

Gray matter heterotopia

‘Focal’ vs ‘Band’ heterotopia

Ellison and Love. Neuropathology 2004
Cortical migrational disorders

Gray matter heterotopia, focal
Cortical migrational disorders

Imaging clues

1. Focal cortical thickening (pachygyria)
2. Abnormal pattern of cortical gyration
3. Indistinct gray-white matter interface
4. Regional or lobar hypoplasia/atrophy
5. Abnormal T2 hyperintensity of gray or white matter
Cortical migrational disorders

Gray matter heterotopia, focal, at 3T

Nat Rev Neurol 2011;7:99
Cortical migrational disorders

Gray matter heterotopia, focal, at 3T

trans-mantle sign
Cortical migrational disorders

Gray matter heterotopia, focal, at 7T
‘tissue-border’ enhancement

SPGR

Epilepsia 2015;epub
Cortical migrational disorders

Gray matter heterotopia, focal, at 7T

SWAN

GRE

Epilepsia 2015;epub
31F with precocious puberty & seizures

T1

T1 (SPGR)
31F with precocious puberty & seizures

hypothalamic (tuber cinereum) hamartoma
Pachygyria: abnormally thick cortical mantle
Lissencephaly: abnormal “smoothness” (lack of normal gyral pattern) of cortex, with or without pachygyria
Lissencephaly: abnormal “smoothness” (lack of normal gyral pattern) of cortex, with or without pachygyria
Cortical migrational disorders

Blumcke (pathologic) classification of FCDs

**Type 1**: FCD with abnormal cortical lamination

**Type 2**: FCD with dysmorphic neurons (balloon cells)

**Type 3**: FCD with architectural distortion of cortex
  a. with hippocampal atrophy
  b. adjacent to glial tumor
  c. adjacent to vascular malformation
  d. adjacent to other early acquired lesions
40M with intractable focal seizures
40M with intractable focal seizures

Focal cortical dysplasia
38F with focal seizures
38F with focal seizures

Subependymal nodular gray matter heterotopia
Cortical migrational disorders

Gray matter heterotopia, multifocal nodular
Cortical migrational disorders

Gray matter heterotopia, band
Polymicrogyria: excessive or redundant abnormal folding of cortical mantle
42M with refractory complex partial epilepsy

T1 (FSPGR)

T1 (FSPGR)

PD
42M with refractory complex partial epilepsy

- T1 (FSPGR)
- Focal polymicrogyria
- PD
Schizencephaly: cavity or cleft lined by heterotopic gray matter, disrupts cortical architecture

(Porencephaly: encephalomalacic cyst or cavity which disrupts cortical architecture)
Schizencephaly with septo-optic dysplasia.

The cleft is lined by heterotopic grey matter.
Septo-optic dysplasia: underdevelopment of optic nerves and absence of septum pellucidum
Septo-optic dysplasia: underdevelopment of optic nerves and absence of septum pellucidum
Mesial temporal sclerosis

MRI features

Main findings: hippocampal atrophy and increased signal intensity on FLAIR and T2; Minor findings: loss of surface and internal structure, atrophy of (extra-)temporal structures (ipsilateral temporal pole, ipsilateral fornix, ipsilateral mamillary body, white matter of the ipsilateral parahippocampal gyrus), decreased signal intensity on T1

Do not miss! Bilateral HS; Dual pathology (HS and extrahippocampal or extratemporal abnormalities); In adults with late-onset epilepsy and progressive neuropsychological decline or psychiatric disease, consider limbic encephalitis.
Medial temporal sclerosis (gliosis & neuronal loss)
Papez circuit (…hippocampus → hypothalamus → thalamus → cingulum → hippocampus…)

Papez JW. A proposed mechanism of emotion. Arch Neurol Psych 1937;38:725
Papez circuit (hippocampus → hypothalamus → thalamus → cingulum → hippocampus...)

Semin Ultrasound CT MRI 2008;29:2
Papez circuit (...hippocampus → hypothalamus → thalamus → cingulum → hippocampus...)
Papez circuit (…hippocampus → hypothalamus → thalamus → cingulum → hippocampus…)

Semin Ultrasound CT MRI 2008;29:2
57F with medically-refractory left temporal complex partial seizures

T1 (SPGR)  
T2-FLAIR

Left mesial temporal sclerosis
41M with left-sided partial seizures

Left mesial temporal sclerosis
Tuberous sclerosis complex (TSC)

giant cell astrocytoma, tubers, sub-ependymal nodules
Sturge-Weber syndrome

leptomeningeal angiomatosis
Neurofibromatosis (NF) type 1

hamartomas (optic glioma, Lisch nodules, café au lait spots)
Summary

Clinical history is key.

Lesions will be missed if they are not suspected or if the correct imaging protocol is not used.