Epileptogenic Focus Detection using PET and Ictal SPECT

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Introduction
The Magnitude of the Problem

- 800,000 Patients Suffer from Epilepsy in the U.S.
- 30-50% are Non-responsive or Poorly Responsive to Medical Management (Intractable Seizures)
- Many Have Multiple Seizures Each Day
- 75,000 Could be Helped by Localization and Neurosurgical Removal of the Seizure Focus
- Many Surgical Candidates are in Their Teens or Pre-teens

Purpose of Brain Imaging in Epilepsy
is to Identify the Epileptogenic Focus

- Ictal Tc-99m HMPAO SPECT
  - Superior in Identifying Extra-Temporal Lobe Foci
    (Increased rCBF)
- Inter-ictal F-18 FDG PET
  - Superior to Inter-ictal SPECT in Identifying Temporal Lobe Epileptogenic Foci
    (Decreased Metabolism)
Confirmatory or Secondary Tests

Inter-ictal Tc-99m HMPAO: Direct Comparison with the Ictal Tc-99m HMPAO SPECT

Inter-ictal F-18 FDG PET: For Extra-Temporal Lobe Epilepsy when an Ictal Tc-99m HMPAO SPECT Scan Cannot be Performed

Ictal rCBF SPECT Method

- 60 mCi Dose Delivered to Epilepsy Unit ~8:00 AM
- Nomogram for Injection, Dose Monitoring, Radiation Safety Approvals
- Trained Personnel Immediately Available (within seconds) to Perform the Ictal Injection Between 8am Until 2pm
- Antiseizure Medication Followed by SPECT Scan at Rest (Reflecting the Ictal Injection State)

Six Bed Video-EEG Monitoring

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Injection of Tc-99m HMPAO During a Seizure
Followed by Rest SPECT Scan (Reflecting Ictal Injection State)

Brain SPECT Performed After Patient is Stabilized

Study of 53 Patients with Refractory Epilepsy

- Ictal scalp EEG was localizing in 66%
- MRI was localizing in 64%
- PET was localizing in 71%
- Ictal SPECT subtraction analysis had 86% sensitivity and 75% specificity
- Intracranial EEG was localizing in 85%

Ictal SPECT

Case Examples

T.M. 9 Y/O M

Clinical
• Onset of Seizures at Age 2.5 Yrs
• Progressing to Frequency Every 20 Minutes
• Partial Complex Type, Involving Left Side of Body

EEG
• Diffuse Localization to Frontal Brain Region

CT and MRI
• CT and MRI Normal

Tc-99m HMPAO Brain Scan (Ictal Injection)
• Intense Focal Hyperemia in Right Dorsal Lateral Frontal Cortex (40% Increase from Normal Value)

T.M. 9 Y/O M  SPECT Scan About 1 Hour Post-Injection

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Location of Ictus on MRI Identified by Fusion SPECT

SPECT-MRI CORRELATION

3D Ictal SPECT aids in placement of subdural EEG electrode grid
T.M. 9 Y/O M Sub-Dural EEG

T.M. 9 Y/O M Radiograph of Subdural Electrodes

T.M. 9 Y/O M EEG Recording Activity

Seizure Free After Surgery

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S.C. 8 Y/O M

- Medically Intractable Seizure Onset at Age 2. Etiology Unknown, Normal Physical Examination.
- MRI: Normal; 18 FDG PET: Normal.
- Ictal Te-99m HMPAO SPECT: Left Mesial Frontal Hyperemia, Propagation over Left Frontal Convexity.
- Surgical Results: Minimal cortical dysplasia. Seizure free 9 Mo post surgery, no neuro deficits.
S.C. 8 Y/O M

Ictal SPECT Propagation Pattern

- Left Frontal Focus
- Left Basal Ganglia Activation
- Right Cerebellar Activation
- (Ipsilateral Basal Ganglia and Contralateral Cerebellar Hemisphere)

Laich E et. al., Supplementary sensorimotor area epilepsy. Seizure localizations, cortical propagation and subcortical activation pathways using ictal SPECT. Brain. 120:855-64, 1997.

S.C. 8 Y/O M

Importance of Anatomic Correlation for Surgery

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E.Z. 5 Month Old Male

- Seizure Semiology: Lips, Arms and Legs Jerking, Which Generalizes, Multiple Times Daily. Clinically, Tonic Followed by Clonic, Head Turn to Left, Followed by Generalization.
- MRI: Normal.
- F-18 FDG PET: Not Performed.
- Ictal Tc-99m HMPAO SPECT: Large Region of Right Dorsal Lateral Frontal Hyperemia. Interictal Tc-99m HMPAO SPECT: Not Performed.
- Surgical Results: Cortical Dysplasia.

E.Z. 5 Mo/O M Ictal SPECT

The Ictal State Shows (Increased rCBF), The Interictal State Shows (Decreased rCBF): More Specific than Ictal Alone.

Ictal and Interictal SPECT

- Comparison of Ictal SPECT with Interictal Baseline SPECT

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M. D. 38 Y/O Male

Clinical:
Intractable Epilepsy

MRI: Normal

Tc-99m HMPAO ictal brain SPECT:
Intense Activity in Right Frontal Lobe

In Cases of Clear Focal Increased rCBF and Normal MRI, a Baseline SPECT is Usually Normal

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T. J. 37 Y/O F

- Hypothalamic Hamartomas (Gelastic Seizures)
- Cognitive Deterioration and Behavioral Problems
L.S. 19 Y/o Male

- Intractable Seizures for 9 Years.
- Left FrontoTemporal Dysplasia
- Patient Underwent Two Ictal SPECT scans and One Interictal SPECT scan.
D.S. 10 Y/O M

- Medically Intractable Seizure Onset at Age 2. Etiology Unknown, Normal Physical Examination.
- **Seizure Semiology:** No Aura. Head and eyes Deviate to the Right. Rhythmic Jerking of the Right Side of the Body. Duration is 90 Minutes. Frequency is Several Seizures a Day.
- **EEG:** Ictal: Right and Left Frontal Spikes. Interictal: Non-Localizing.
- **MRI:** Normal.
- **F-18 FDG PET:** Not Performed.
- **Two Ictal Tc-99m HMPAO SPECT:** First Ictal SPECT Consistent with Right or Left Frontal Lobe Focus.
- **Repeat Ictal SPECT:** Localizing to Left Dorsal-Lateral Frontal Region.

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D.S. 10 Y/O M  
**First Ictal SPECT**

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D.S. 10 Y/O M  
**Repeat Ictal SPECT**

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S.P. 2 Y/O M

Intractable epilepsy.
Seizures began 3 days after birth.

MRI scan: No atrophy or signal change to suggest the location of epileptogenesis.

Interictal and ictal Tc-99m HMPAO brain SPECT scans were performed.

**Interictal Scan:**
The primary epileptogenic focus possibly is localized in the right fronto-polar region (low rCBF, suggestive but not specific).

**Ictal Scan:**
The primary epileptogenic focus is localized in the right fronto-polar region (high rCBF is more specific with an interictal scan).
J.P. 9 Y/O F Intractable Seizures Since Age 1

MRI: Left temporal-parietal developmental malformation.

Inter-ictal SPECT:
Primary epileptogenic focus possibly is in the left temporal lobe (shows reduced left temporal and parietal lobe rCBF and crossed cerebellar diaschisis).

Ictal SPECT:
Confirms that the primary epileptogenic focus is localized in the left temporal lobe.
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Left Temporal-Parietal Developmental Malformation

J.P. 9 Y/O F

Tc-99m HMPAO SPECT

low rCBF

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Ictal and Interictal SPECT
Comparison with analyze and SPM

• Automated Registration and Normalization with Statistical Image Mapped onto MRI or Interictal SPECT
• Analyze AVW or SPM2 Algorithms

Registration Aligns Functional Scan to Anatomic Scan

Statistical Correlation Methods

- Normalized Co-aligned

Ictal
Interictal

Analyze SPM
+ 2S.D.
L.C. 40 year old right handed male

- History of complex partial medically intractable seizures since age of 5.
- Typical seizures is sudden, brief, ~15 sec period of startled and confused state, 2 to 3 times per day.
- Post seizure he demonstrated bizarre behavior.
- Repetitive, well coordinated, semi-purposeful movements involving the face, lips, hands and feet (e.g. facial grimacing, puckering of mouth, shaking hands).
- Video-EEG monitoring which was non-localizing.

A 3 x 7 cm grid for subdural electrode placement was performed on right frontal lobe overlying seizure focus identified on Ictal SPECT.

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Cingulate Gyrus Epilepsy

Ictal SPECT Compared to Normal Using Statistical Parametric Mapping (SPM)
Interictal F-18 FDG PET Scan

- Performed Routinely as Outpatient
- More Accurate than Interictal Tc-99m HMPAO SPECT for Temporal Lobe Epilepsy or Non-Temporal Seizures
- Can be Performed for Non-Temporal Lobe Epilepsy when Ictal SPECT is not Possible

Method: Interictal F-18 FDG PET

- Patient Placed in a Comfortably Recliner, in Dimly lit Room with Minimal Ambient Noise to Decrease Stimulation of the Brain.
- IV injection of ~ 10 mCi F-18 FDG
- Incorporation Time of 30 Minutes
- PET Interpreted as Localizing if a Definite Region of Hypometabolism is Seen (Suggest Review of MRI and Clinical History)
New Onset Seizure Disorder

MRI: Right Temporal Pole Abnormality
(Question of High Grade Tumor Raised).

F-18 FDG PET: No Hypermetabolic Area to
Suggest the Presence of a Malignant Lesion in
the Right Temporal Lobe.

MRI: Right Temporal Pole
Increased Signal Intensity

F-18 FDG PET:
Right Temporal Pole Hypometabolism
Case: J.R. 41 y/o M

Clinical: Patient with Intractable Complex Partial Seizures being Evaluated For Epilepsy Surgery.

Video-EEG monitoring: Non-Localizing
MRI: Mild Decrease in Size of Left Hippocampus
Inter-ictal SPECT: Normal
18 FDG PET: Decreased Uptake by the Left Temporal Lobe c/w Left Temporal Lobe Epilepsy.

C. P. 26 Y/O F With Seizure Disorder

Clinical: Patient with Intractable Complex Partial Seizures being Evaluated For Epilepsy Surgery.

Video-EEG monitoring: Non-Localizing
MRI: Mild Decrease in Size of Left Hippocampus
Inter-ictal SPECT: Normal
18 FDG PET: Decreased Uptake by the Left Temporal Lobe c/w Left Temporal Lobe Epilepsy.

C. P. 26 Y/O F: Smaller Left Temporal Lobe
History of Intractable Complex Partial Seizures Since Childhood With Secondary Generalization.

MRI: Normal.

F-18 FDG PET: Left Temporal Lobe Seizure Foci Detected by Reduction of F-18 FDG.
MRI: Normal (Coronal)

FF-18 FDG PET: Inter-ictal (L. TLE)

W.R. 25 Y/O F

- Medically Refractory Complex Partial Seizures.
- MRI: Normal.
- F-18 FDG PET: Left Temporal Lobe Epilepsy Hypometabolism (Hippocampal Region).
W.R. 25 Y/O F  F-18 FDG Brain PET: Left TLE

D.R. 16 Y/O F

- Refractory Complex Partial Seizures.
- MRI: Normal.
- F-18 FDG PET: Left Temporal Lobe Epilepsy
  Hypometabolism (hippocampal region).
D.R. 16 Y/O F  Left Temporal Lobe Epilepsy

Ictal and Interictal SPECT and Interictal F-18 FDG PET

- Provides Complementary Information
- Both Approaches Assist to Confidently Determine the Epileptogenic Focus

A.R. 15 Y/O F with Intractable Seizures

Clinical: 1-2 Seizures/Day
Video-EEG monitoring: Non-Localizing
MRI: Normal

Ictal Tc-99m HMPAO:
Focal Intense Right Frontal Hyperperfusion

Inter-ictal F-18 FDG PET:
Subtle Right Frontal Hypometabolism, Confirmatory but Non Localizing

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A.R. 15 Y/O F  Normal MRI

A.R. 15 Y/O F  Tc-99m HMPAO Ictal SPECT and Inter-Ictal F-18 FDG PET

A.R. 15 Y/O F  Tc-99m HMPAO Ictal SPECT and F-18 FDG PET

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K.S. 21 Y/O F

F-18 FDG PET:
No area of decreased F-18 FDG uptake to suggest the location of the epileptogenic focus.

Inter-ictal Tc-99m HMPAO SPECT Scan:
A useful baseline for comparison with ictal SPECT.

Ictal Tc-99m HMPAO SPECT Scan:
The seizure focus is in the left mesial frontal region.

K.S. 21 Y/O F

Normal MRI

K.S. 21 Y/O M

Tc-99m HMPAO SPECT

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K.S. 21 Y/O F  Tc-99m HMPAO SPECT

K.S. 21 Y/O F  F-18 FDG PET and Tc-99m HMPAO Ictal SPECT

K.S. 21 Y/O F  F-18 FDG PET and Tc-99m HMPAO Ictal SPECT
D.M. 43 Y/O M.

History of medically intractable seizures.

MRI scan normal.

Tc-99m HMPAO Ictal SPECT:
Increased rCBF in the right parasagittal frontal lobe.

F-18 FDG PET Scan:
Decreased F-18 FDG uptake in the right parasagittal frontal lobe.

D.M. 43 Y/O M  Ictal Tc-99m HMPAO SPECT

D.M. 43 Y/O M  F-18 FDG PET

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Intractable seizures since age 12.

**MRI Scan:** Non-Lateralizing.

**PET Scan:** Subtle decrease in F-18 FDG uptake in the right parietal lobe.

**Inter-ictal SPECT:** Non-Lateralizing.

**Ictal SPECT:** The primary epileptogenic focus is located in the right cerebral hemisphere (Fronto-temporal and Parietal Lobes).
R.W., 31 Y/O M
F-18 FDG PET

R.W., 31 Y/O M
F-18 FDG PET and Tc-99m HMPAO ictal SPECT

R.W., 31 Y/O M
F-18 FDG PET and Tc-99m HMPAO ictal SPECT

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The patient with a history of medically intractable seizures.

MRI scan normal.

Ictal Tc-99m HMPAO SPECT
Increased rCBF in the right temporal lobe.

F-18 FDG PET
Reduction of F-18 FDG in right temporal lobe.
Intractable seizures, surgical candidate.

**CT scan:**
Right frontal sclerosis.

**Ictal SPECT:**
Focus in the right parasagittal frontal lobe.

**FDG PET:**
Focus in the right parasagittal frontal lobe.

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Summary

- Scalp EEG Recordings Have Low Spatial Resolution.
- Ictal SPECT: Epileptogenic Foci have High rCBF (Greater Accuracy Compared with Other Methods).
- Interictal SPECT: Epileptogenic Foci have only slightly low rCBF (Used for Confirmation of Ictal SPECT).
- Interictal PET: F-18 FDG Used to Localize Temporal Lobe Foci (Mesial Temporal or Hippocampal Sclerosis/Atrophy) and Other Cortical Regions.
- Ictal PET: F-18 FDG PET Cannot be Used Due to Long Incorporation Time of FDG and Short Seizure Duration.