CNS Radiopharmaceuticals

Original presentation by: Vicky Nguyen MD
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Reviewed by: Manuela Matesan MD
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Clinical Indications for Cerebral Scintigraphy

- Dementia
  - Alzheimer’s disease
  - Lewy Body disease
  - Pick’s disease
  - Multi-infarct dementia
  - AIDS-dementia complex
- Epilepsy
- Stroke
- Transient Ischemia Attacks
- Head Trauma
- Movement Disorders
- Parkinson’s disease
- Huntington’s chorea
- Psychiatric Disorders
  - Attention deficit disorder
  - Obsessive compulsive disorder
  - Schizophrenia
- Brain Death
- Tumor Imaging
Blood Brain Barrier

• Non-Diffusible
  • Hydrophilic and polar
  • cannot cross BBB unless abnormal tissue
  • $^{99m}$TcO$_4^-$, $^{201}$Tl, $^{99m}$Tc-DTPA

• Diffusible
  • lipophilic
  • readily cross BBB
  • $^{99m}$Tc-HMPAO, $^{99m}$Tc-ECD, 18F-FDG
Brain SPECT and PET Radiopharmaceuticals Used Clinically

• Blood-brain barrier
  • Tc-99m glucoheptonate
  • Tc-99m DTPA
• Brain perfusion
  • I-123 iodoamphetamine
  • Tc-99m HMPAO
  • Tc-99m ECD
• Metabolism
  • F-18 fluorodeoxyglucose
• Brain tumor imaging
  • Thallium-201
  • Tc-99m sestamibi
  • F-18 FDG

• Cisternography
  • In-111 DTPA
• Shunts
  • Tc-99m pertechnetate
Brain Perfusion Scan
Tc-99m HMPAO
# FDA-Approved Radiopharmaceuticals

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Approved Indications</th>
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<tbody>
<tr>
<td>Fluorine-18 fluorodeoxyglucose</td>
<td>PET: abnormal glucose metabolism in oncology and foci of epileptic seizures</td>
</tr>
<tr>
<td>Florbetapir, florbetaben, Flutemetamol</td>
<td>Estimate β-amyloid neuritic plaque density</td>
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<td>Indium-111 pentetate</td>
<td>Cisternography</td>
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<td>Iodine-123 ioflupane (DaTscan)</td>
<td>Striatal dopamine transporter visualization</td>
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<td>Iodine-123 human serum albumin</td>
<td>Localization of cerebral neoplasms</td>
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<td>Technetium 99m bicisate (Neurolite)</td>
<td>Localization of stroke</td>
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<tr>
<td>Technetium 99m exametazine (Ceretec)</td>
<td>Localization of stroke</td>
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<tr>
<td>Xenon-133 gas</td>
<td>Cerebral flow</td>
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SPECT Agents

- Regional cerebral brain perfusion
- Correlates well with function of brain
  - Greater blood flow required by areas of greater synaptic activity
- Tc-99m ECD and Tc-99m HMPAO
  - Neutral, lipophilic – passive diffusion across BBB
  - High first pass extraction
Tc-99m ECD
- Parietal, occipital lobes
- $1^{\text{st}}$ pass extraction: 60-70%
  - 5-6% localized
- Crosses BBB $\rightarrow$ enzymatic de-esterification
- More rapid blood clearance
- Slow washout (6% per hour)

Tc-99m HMPAO
- Frontal lobes, thalamus, cerebellum
- $1^{\text{st}}$ pass extraction: 80%
  - 3.5-7% localized w/in 1 min
- Crosses BBB $\rightarrow$ polar hydrophilic molecule
- 15% wash out first 2 min, little loss next 24 hr
  - SPECT image 15 min-2hr
$^{99m}$Tc-ECD Brain SPECT Ictal/Interictal Study

- Increased ictal uptake within right temporal lobe consistent with an epileptogenic focus within the right hemisphere, most prominent in the right temporal lobe.
# Tracer Uptake Patterns

<table>
<thead>
<tr>
<th>Tracer Uptake Pattern</th>
<th>Cause</th>
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<tbody>
<tr>
<td>COLD (no uptake)</td>
<td>CSF</td>
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<td></td>
<td>Edema</td>
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<td></td>
<td>Necrosis</td>
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<td></td>
<td>Space-occupying lesions (hemorrhage, tumors, cysts, AVM, postsurgery)</td>
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<tr>
<td>HYPOACTIVE (decreased uptake)</td>
<td>Ischemia</td>
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<tr>
<td></td>
<td>Hypometabolism (hypofunction): degeneration, deafferentation</td>
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<tr>
<td></td>
<td>Atrophy</td>
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<tr>
<td>HYPERACTIVE (increased uptake)</td>
<td>Luxury perfusion</td>
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<tr>
<td></td>
<td>Encephalitis</td>
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<td></td>
<td>Acetazolamide-induced vasodilation</td>
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<tr>
<td></td>
<td>Hyperfunction (epilepsy [ictal], neuroactivation, etc)</td>
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<td></td>
<td>Tumors</td>
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Acetazolamide

• Assess cerebrovascular reserve capacity of the brain
• Identifies areas at highest risk of ischemia
$^{18}$F-Fluorodeoxyglucose

- Crosses BBB by glucose transporter system
- Metabolized in brain cells
  - FDG is phosphorylated into FDG-6-phosphate
- FDG-6-phosphate
  - Does not undergo further metabolism because it lacks hydroxyl group at the 2-position
  - Remains trapped in brain for several hours due to negative charge
- $^{18}$F-FDG PET studies: epileptic foci, tumor, dementia, recurrent tumor vs radiation necrosis
Iodine-123 ioflupane (DaTscan)

- Approved by FDA in January 2011
- Detects dopamine transporters
- Help differentiate essential tremor from tremors from parkinsonian syndromes
- Cannot distinguish PD from atypical PD

Figure 13-22  Dopamine neuron production and metabolism. The sites of PET and SPECT agent uptake are shown. AAAD, Aromatic amino acid decarboxylase; VMAT2, vesicular monoamine transporter type 2; DAT, dopamine reuptake transporter.
DaTscan

NORMAL

ABNORMAL
Cisternography

• Investigation of rate of formation, flow, and resorption of CSF

• Agents:
  • $^{111}$In-DTPA

http://www.control.tfe.umu.se/lan/CSF/CSF_diagram.jpg
CSF leak study In-III DTPA

- SPECT imaging of the head shows a small area of radiotracer extravasation in the left anterior skull base, just lateral to the midline.
- SPECT and pledget counting indicate small CSF leak in the region slightly left to the midline in the left superior nasal cavity.

Pledgets/serum counts ratio:
Rt superior pledget 2.1
Rt inferior pledget 1.6
Lt superior pledget 4.0
Lt inferior pledget 2.1
## Glance at PET Radiopharmaceuticals

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<th>Compound</th>
<th>Application</th>
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<tr>
<td>O-15 H₂O</td>
<td>Blood flow</td>
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<tr>
<td>O-15 O₂</td>
<td>Oxygen metabolism/flow</td>
</tr>
<tr>
<td>O-15 or C-11 carboxyhemoglobin</td>
<td>Blood volume</td>
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<tr>
<td>C-11 methionine</td>
<td>Amino acid metabolism</td>
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<tr>
<td>C-11 methylpiperone</td>
<td>Dopamine receptor activity</td>
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<td>C-11 carfentanil</td>
<td>Opiate receptor activity</td>
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<td>C-11 flunitrazepam</td>
<td>Benzodiazepine receptor activity</td>
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<tr>
<td>C-11 scopolamine</td>
<td>Muscarinic cholinergic receptors</td>
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<td>C-11 ephedrine</td>
<td>Adrenergic terminals</td>
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<tr>
<td>F-18 fluorodeoxyglucose (FDG)*</td>
<td>Glucose metabolism</td>
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<tr>
<td>F-18 fluoro-L-dopa*</td>
<td>Presynaptic dopamine system</td>
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<tr>
<td>F-18 fluorothymidine (FLT)</td>
<td>DNA synthesis</td>
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