

UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE



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Division of Nuclear Medicine
Didactic



CNS Radiopharmaceuticals

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Presentation date: September 2011

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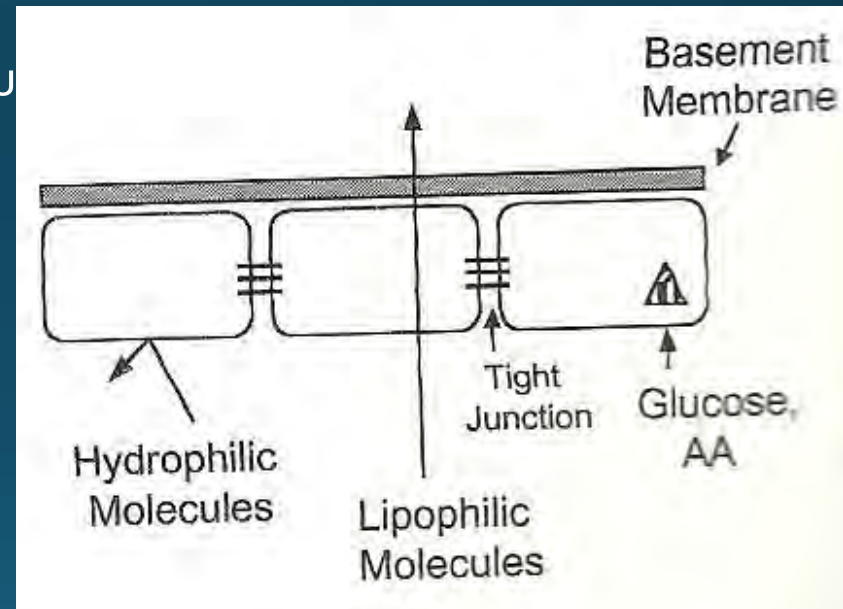
Last update: March 2016

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

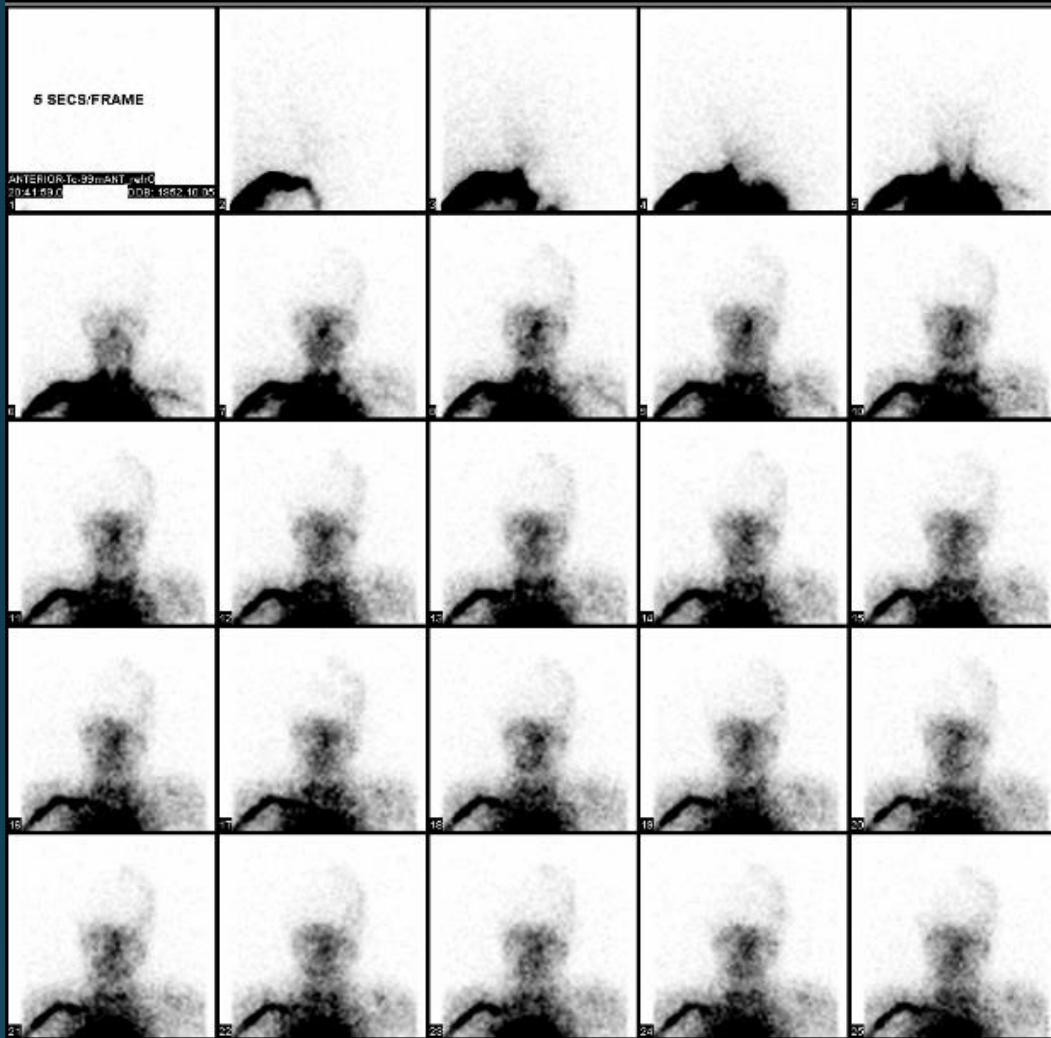
Blood Brain Barrier

- Non-Diffusible
 - Hydrophilic and polar
 - cannot cross BBB unless abnormal tissue
 - $^{99m}\text{TcO}_4^-$, ^{201}Tl , $^{99m}\text{Tc-DTPA}$
- Diffusible
 - lipophilic
 - readily cross BBB
 - $^{99m}\text{Tc-HMPAO}$, $^{99m}\text{Tc-ECD}$, $^{18}\text{F-FDG}$



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

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

SPECT Agents

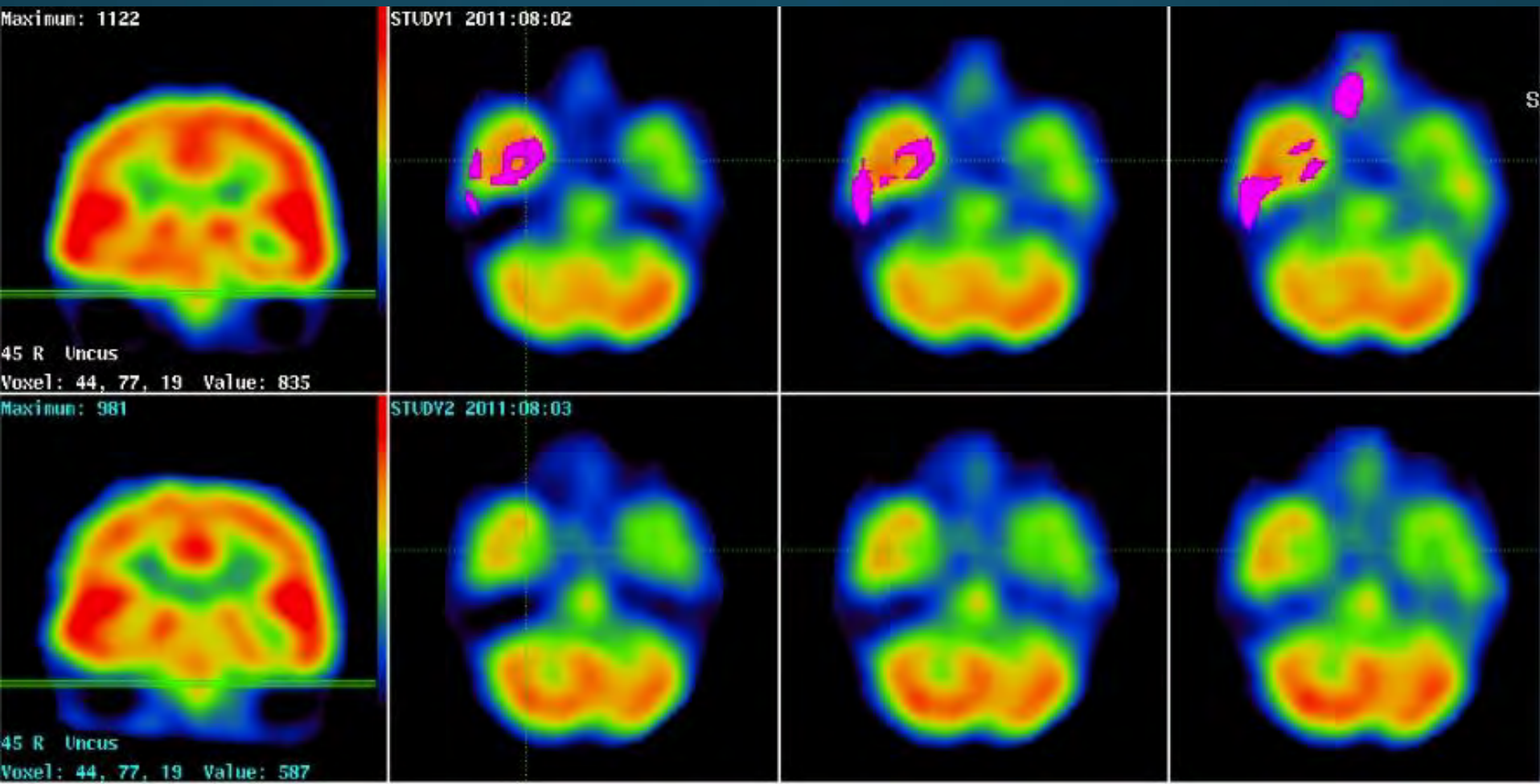
- Regional cerebral brain perfusion
- Correlates well with function of brain
 - Greater blood flow required by areas of greater synaptic activity
- Tc-99m ECD and Tc-99m HMPAO
 - Neutral, lipophilic – passive diffusion across BBB
 - High first pass extraction

Tc-99m ECD

- Parietal, occipital lobes
- 1st pass extraction: 60-70%
 - 5-6% localized
- Crosses BBB → enzymatic de-esterification
- More rapid blood clearance
- Slow washout (6% per hour)

Tc-99m HMPAO

- Frontal lobes, thalamus, cerebellum
- 1st pass extraction: 80%
 - 3.5-7% localized w/in 1 min
- Crosses BBB → 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

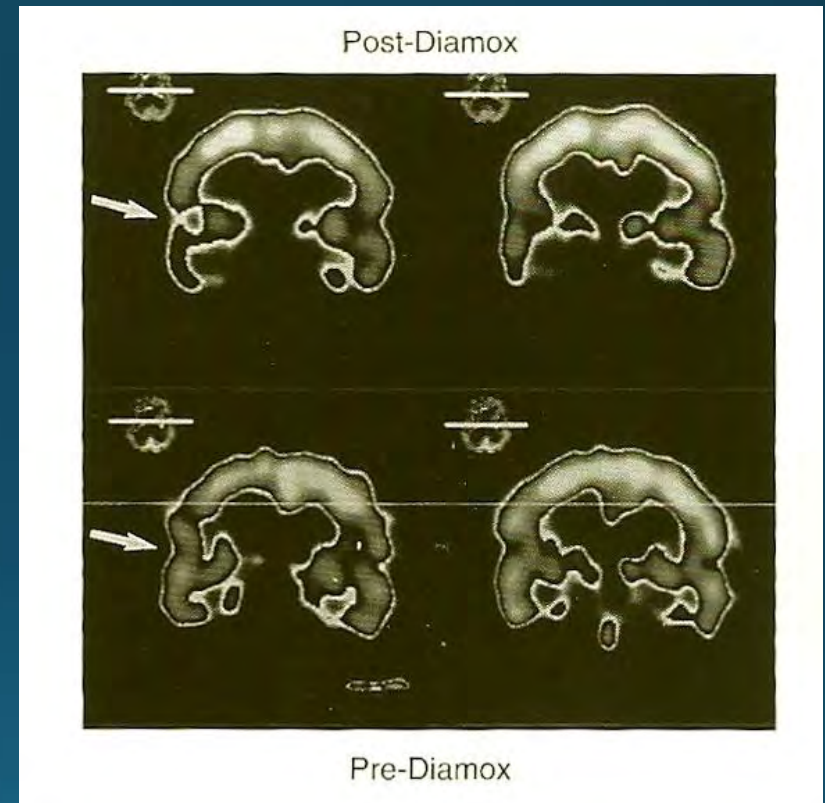
- Increased ictal uptake within right temporal lobe consistent with an epileptogenic focus within the right hemisphere, most prominent in the right temporal lobe.

Tracer Uptake Patterns

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

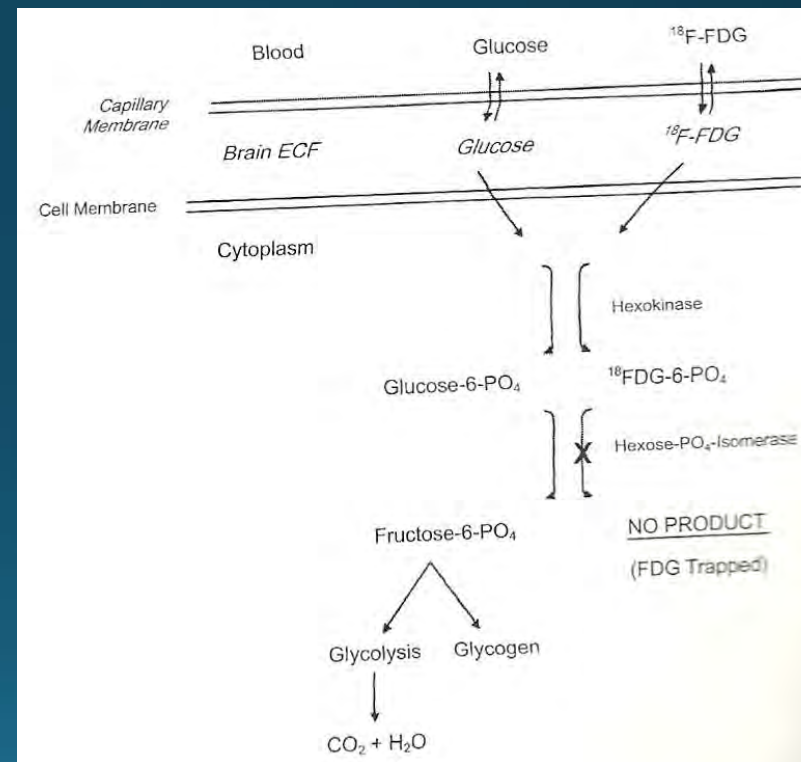
Acetazolamide

- 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

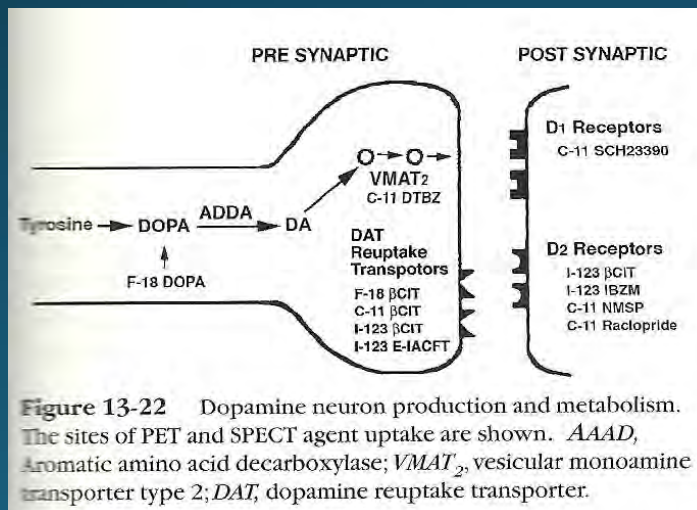
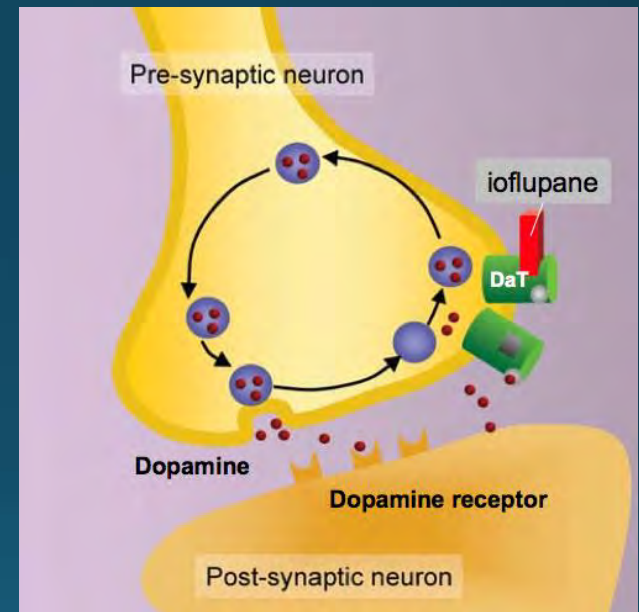
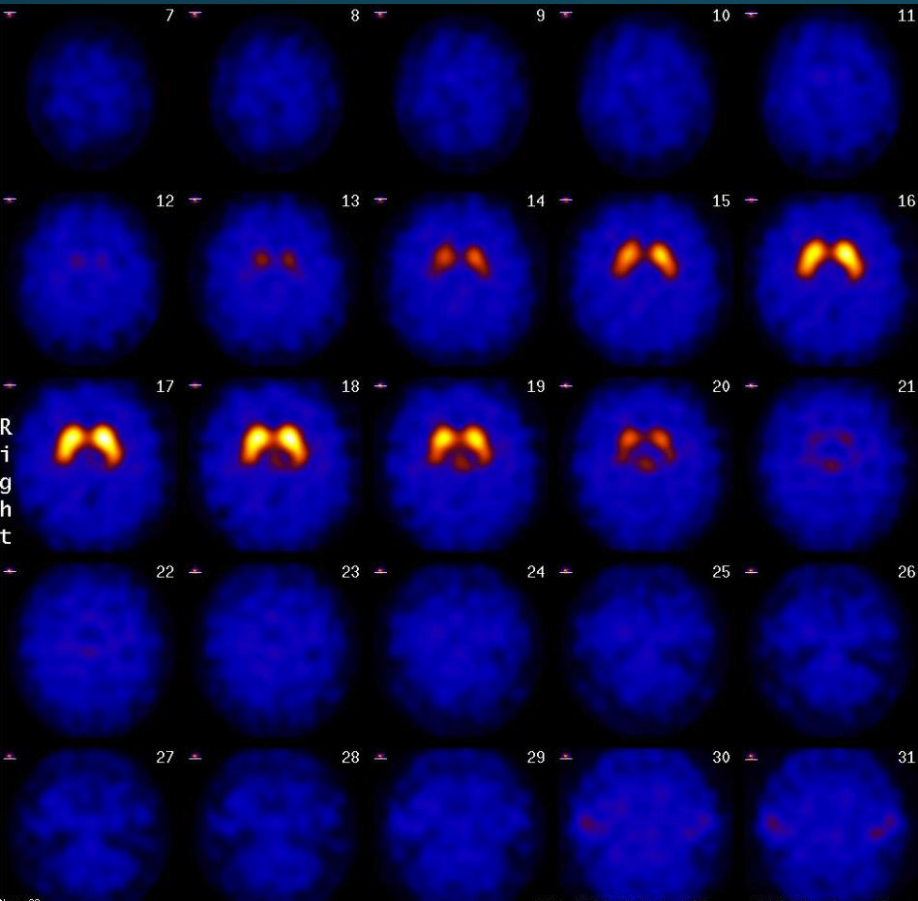


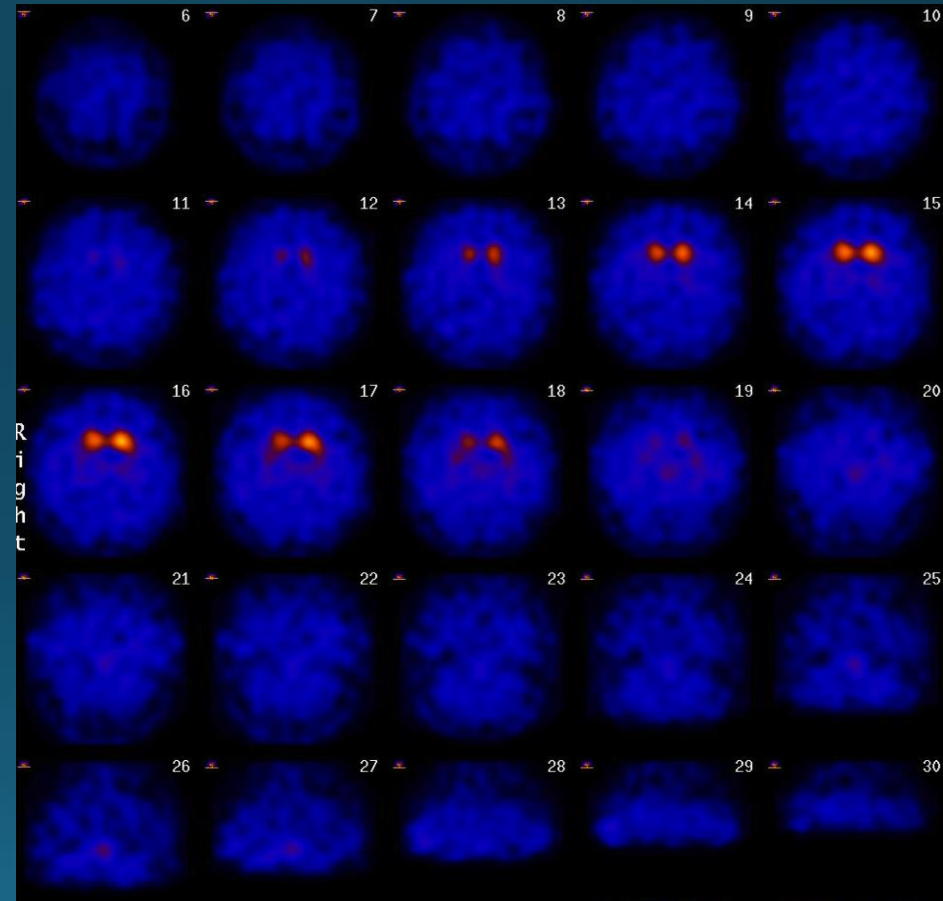
Figure 13-22 Dopamine neuron production and metabolism. The sites of PET and SPECT agent uptake are shown. *AADC*, Aromatic amino acid decarboxylase; *VMAT₂*, vesicular monoamine transporter type 2; *DAT*, dopamine reuptake transporter.

DaTscan

NORMAL

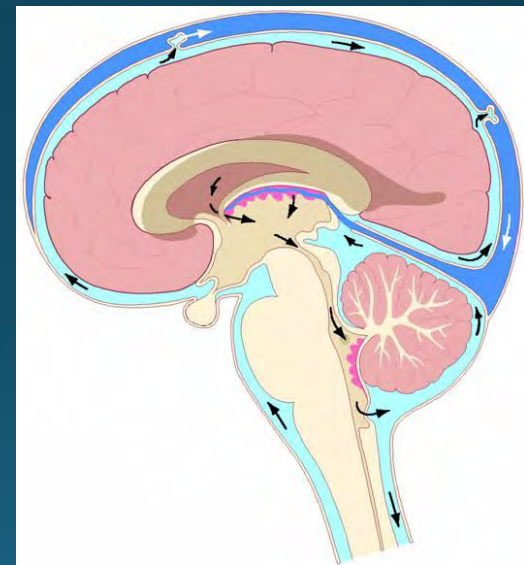
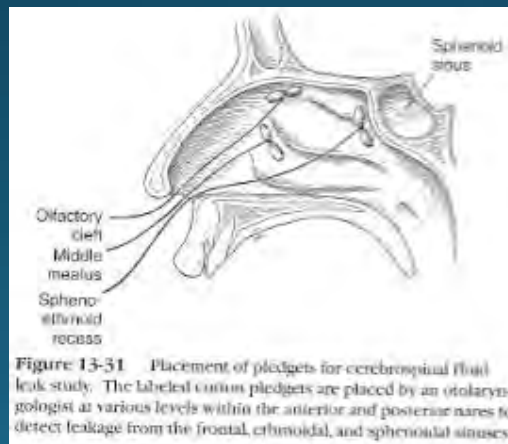
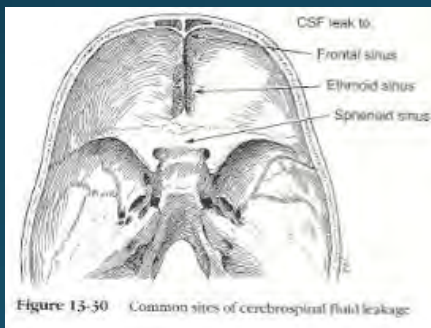


ABNORMAL

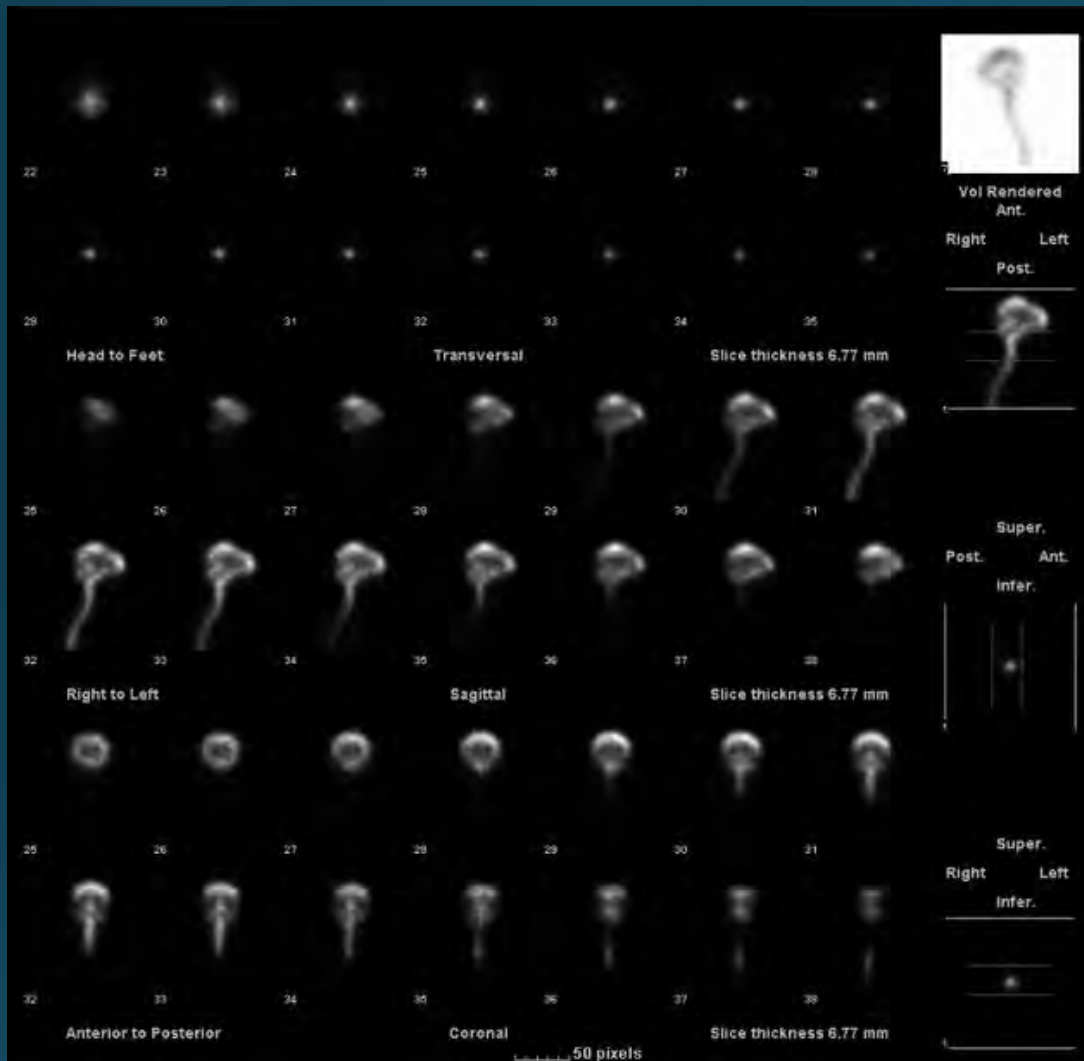


Cisternography

- 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



Pledgets/serum counts ratio:

Rt superior pledget	2.1
Rt inferior pledget	1.6
Lt superior pledget	4.0
Lt inferior pledget	2.1

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.

Glance at PET Radiopharmaceuticals

Compound	Application
O-15 H ₂ O	Blood flow
O-15 O ₂	Oxygen metabolism/flow
O-15 or C-11 carboxyhemoglobin	Blood volume
C-11 methionine	Amino acid metabolism
C-11 methylpiperone	Dopamine receptor activity
C-11 carfentanil	Opiate receptor activity
C-11 flunitrazepam	Benzodiazepine receptor activity
C-11 scopolamine	Muscarinic cholinergic receptors
C-11 ephedrine	Adrenergic terminals
F-18 fluorodeoxyglucose (FDG)*	Glucose metabolism
F-18 fluoro-L-dopa*	Presynaptic dopamine system
F-18 fluorothymidine (FLT)	DNA synthesis

Suggested Articles

1. Catafau, AM. Brain SPECT in Clinical Practice. *J Nucl Med*. 2001;42:259-271.
2. Kowalsky RJ and Falen SW. *Radiopharmaceuticals in Nuclear Pharmacy and Nuclear Medicine*. 2nd ed. Washington DC: American Pharmacists Association; 2004.
3. Krasnow A. The Lost Art of Cerebral Spinal Fluid Nuclear Medicine Annual 2004.
4. **Booth TC. The role of functional dopamine-transporter SPECT imaging in parkinsonian syndromes, part 1.** [AJNR Am J Neuroradiol](#). 2015 Feb;36(2):229-35. doi: 10.3174/ajnr.A3970. Epub 2014 Jun 5.