

# SPECT and PET Imaging: DaT Scan, Cerebral Blood Flow and Epilepsy

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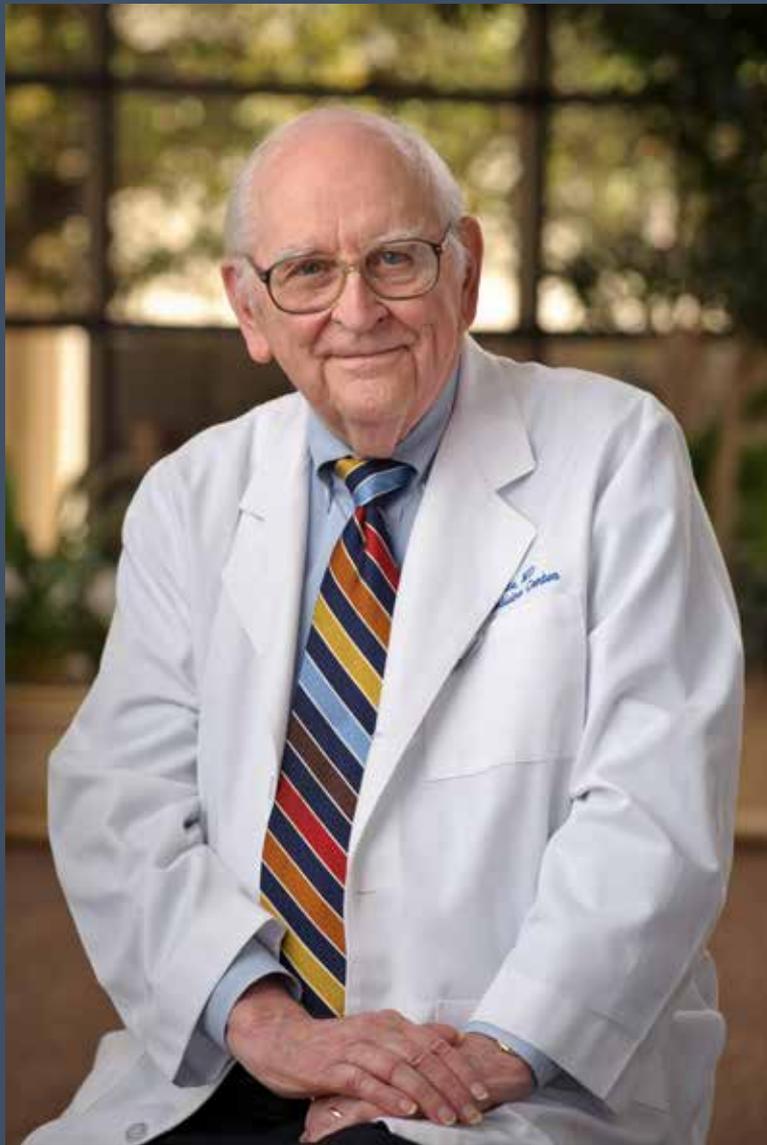
# Financial Disclosures/ Conflicts of Interest/FDA off Label

§ No financial disclosures

§ No COI

§ FDA discussion of drugs not yet approved: F18 AV 133

(VMAT scan)



Frederick J. Bonte, M.D. 1922-2016

# SAMs Objectives

- § Individuals attending this session will at the end of the session be able to
  - § Describe how DATScan may be used to distinguish etiologies of tremor
  - § Restate Uses of SPECT perfusion imaging in cerebrovascular disease and epilepsy
  - § Describe how FDG PET brain imaging may be useful in seizure localization in epilepsy

# Parkinson's Disease (PD)

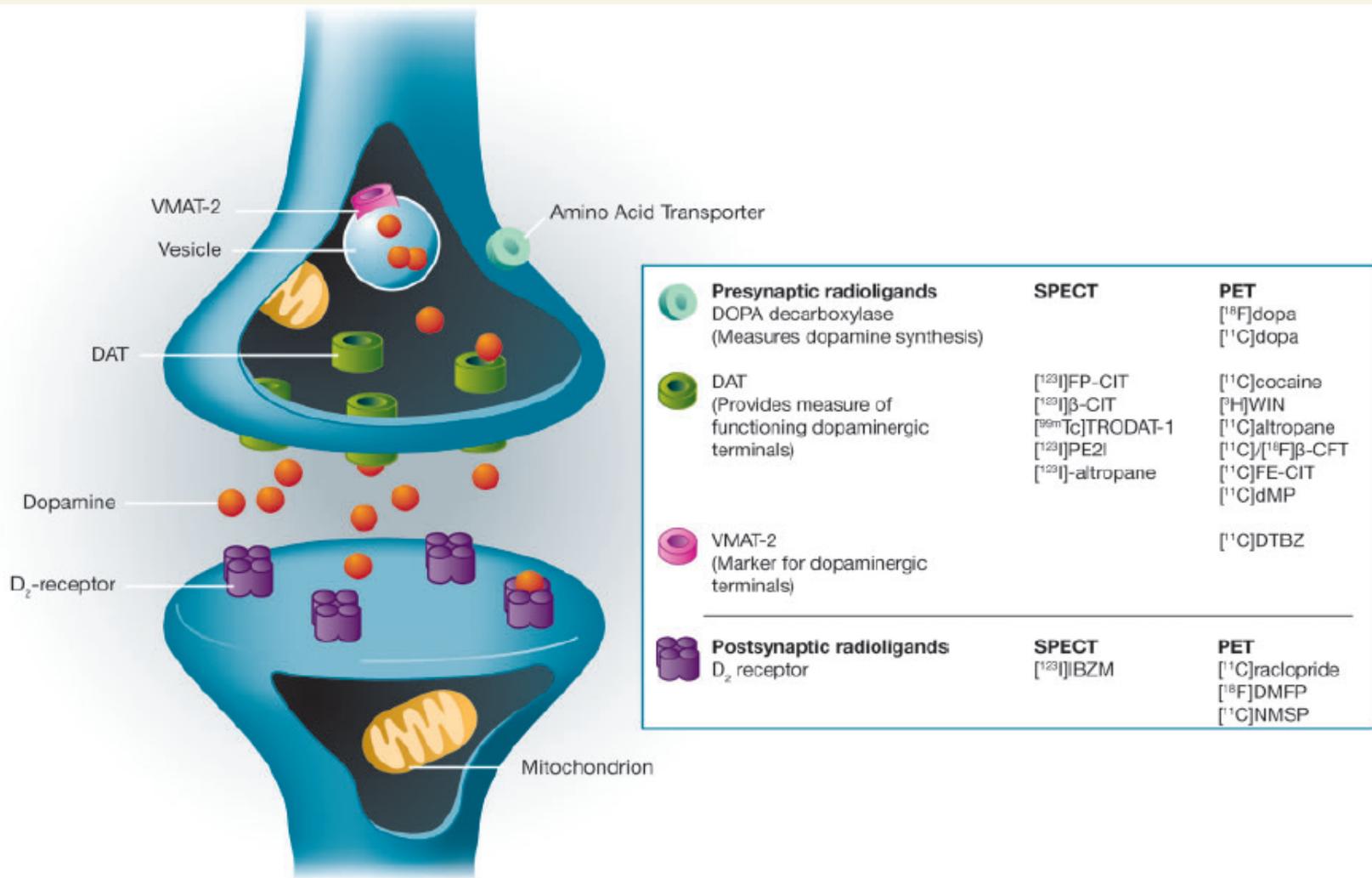
- § Neurodegenerative disorder whose symptoms may include, tremor, rigidity, postural instability, abnormal gait and in some cases dementia
- § Often difficult to diagnose in early stages and the tremor can be mistaken for other causes of tremor, most commonly essential tremor (ET). There are high false positive and false negative rates for each of these diagnoses based on clinical diagnosis alone, even among movement disorder experts.
- § PD is treated with a variety of medications whose goal is provide DA. These medications are ineffective for ET and may exacerbate ET.
- § DaTscan can help distinguish between these two diagnoses (often with higher concordance in NM reading experts than clinical experts)

# Other Disorders in the Parkinsonian Syndromes

- § Progressive supranuclear palsy (PSP)
- § Corticobasal Degeneration (CBD)
- § Multisystem Atrophy (MSA)
- § All these share with idiopathic PD loss of DA neurons but differ in other symptoms and are much less common

# Drug Induced Parksonian Symptoms

- § Very common cause of misdiagnosis
- § Results from pharmacologic agents that block DA receptors but don't affect DAT
- § Common drugs include neuroleptics (eg prochlorperazine, and metoclopramide), and calcium channel blockers
- § DIP more common in women and elderly and does not clearly relate to dosage or length of usage
- § DATScan will look normal !



**Figure 1** Dopaminergic radioligands for SPECT and PET. β-CFT = 2β-carbomethoxy-3β-(4-fluorophenyl)tropane; DAT = dopamine transporter; dopa = dihydroxyphenylalanine; DMFP = desmethoxyfallypride; dMP = d-threo methylphenidate; DTBZ = dihydrotetrabenazine; FE-CIT = (N-(2-fluoroethyl)-2β-carbomethoxy-3β-(4-iodophenyl)nortropane; IBZM = iodobenzamide; NMSP = 3-N-methylspiperone; PE2I = N-(3-iodoprop-(2E)-enyl)-2β-carboxymethoxy-3β-(4'-methylphenyl)nortropane; TRODAT-1 = [2-[[2-[[[3-(4-chlorophenyl)-8-methyl-8-azabicyclo]3.2.1]oct-2-yl]methyl](2-mercaptoethyl)amino]ethyl]amino]ethanethiolato(3-)-N2,N20,S2,S20]oxo-[1R-(exo-exo)]; VMAT = vesicular monoamine transporter; WIN = WIN 55,212-2 cannabinoid receptor agonist.

# DaTScan ( <sup>123</sup>I loflupane)

- § Images presynaptic dopamine transporters (DAT) whose function is retrieve the neurotransmitter dopamine from the synaptic cleft of dopaminergic neurons
- § In Parkinson's Disease and other Parkinsonian disorders, dopamine is severally depleted, resulting in a lower number of nigrostriatal nerve terminals, with subsequent down regulation in DAT
- § DaTscan is a cocaine analogue with high affinity and high selectivity for DAT with greatest uptake in the caudate and putamen

# Imaging with I 123 ioflupaine DATScan

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- § Referring physician prescribes thyroid blockade solution or tablets
- § Referring physician decides which medications should be held prior to scanning
- § On day of scan, patient takes thyroid blocking medication 1 hour prior to injection
- § Patient injected slowly with 5mCi I 123 ioflupane  
Hydrate well and continue to do so for next 48 hrs

# Medications Affecting Imaging

- § Either 100mg potassium iodide or 400 mg potassium chlorate-blocks I 123 uptake in thyroid
- § Amoxapine, amphetamine, benztropine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, norephedrine, phentermine, phenylpropanolamine, selegiline, sertraline, citalopram and paroxetine may interfere with imaging (should be discontinued for scan)

# Imaging with DaTScan

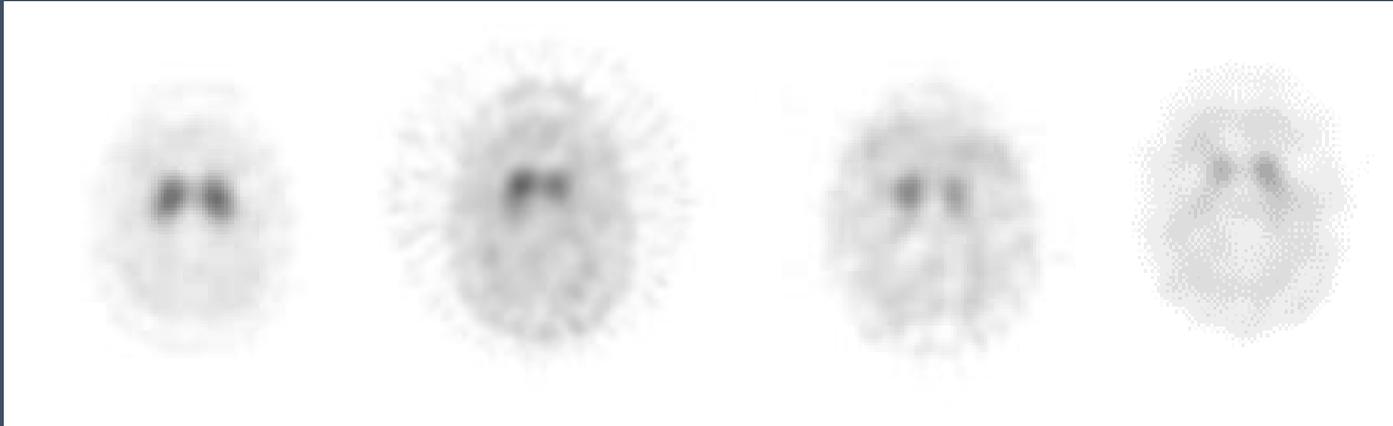
- § After 3 hour uptake, patient images are acquired for approximately 30 minutes
- § 13 cm to no greater than 15 cm distance from patient to collimator
- § Fan beam collimators \*
- § 5 five minute dynamic tomos are acquired for 180 degrees of rotation
- § 128x128 matrix

# Processing Parameters for DATscan

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- § Filtered backprojection
- § Butterworth Filter
- § Order 8 cut off 0.46 on Siemens scanner
- § No Masking

# Interpretation of DaTscan



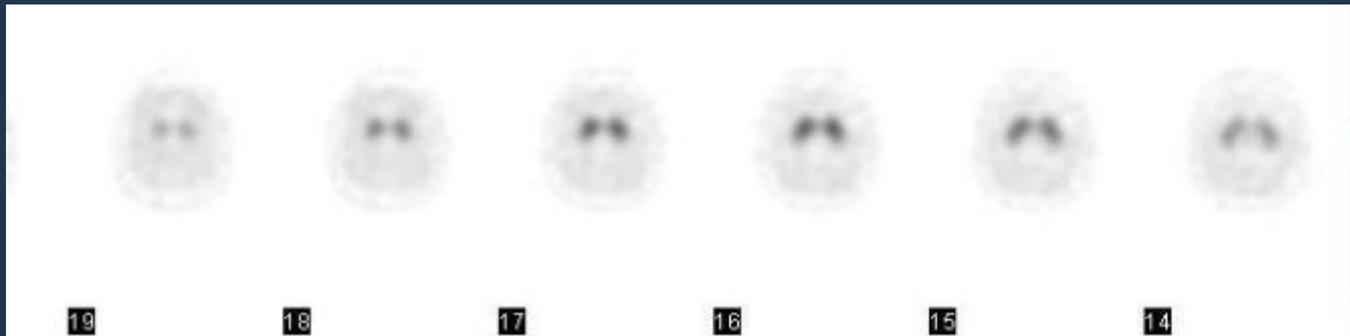
Normal

Grade 1

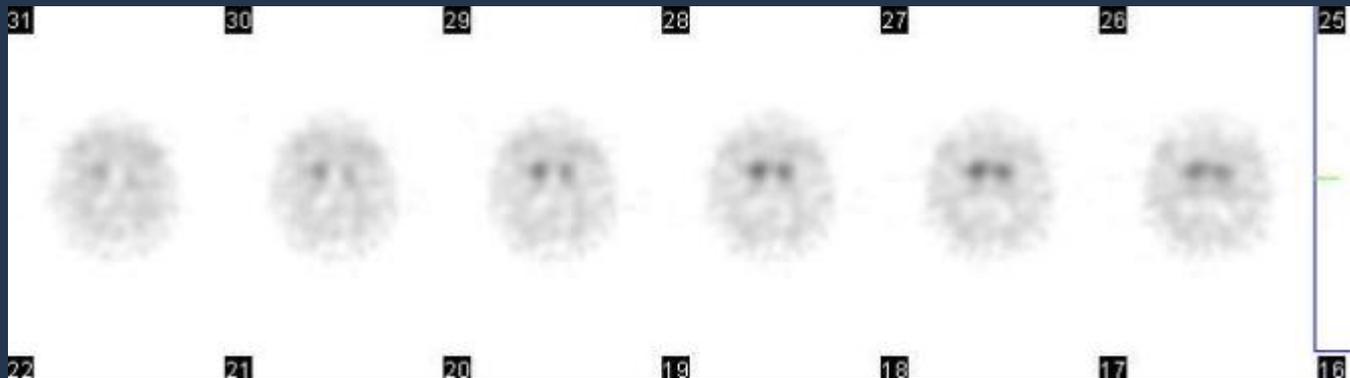
Grade 2

Grade 3

# DATScan | 123 Ioflupane

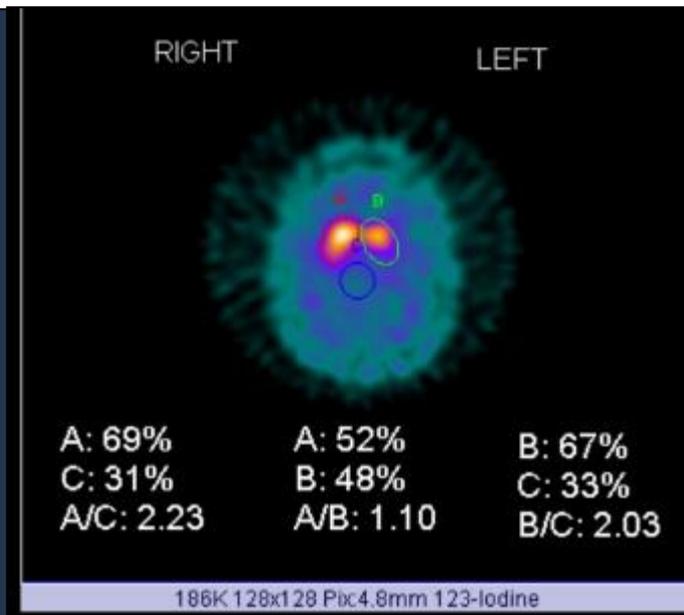
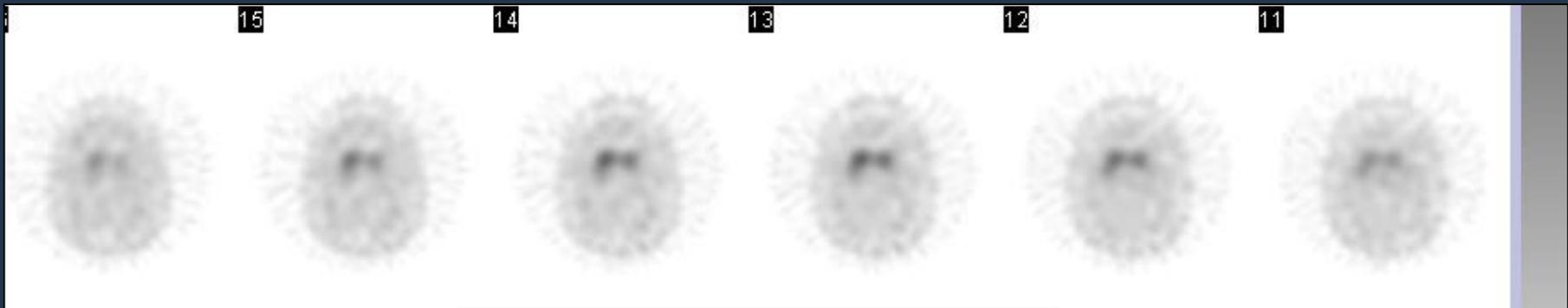


Not PS

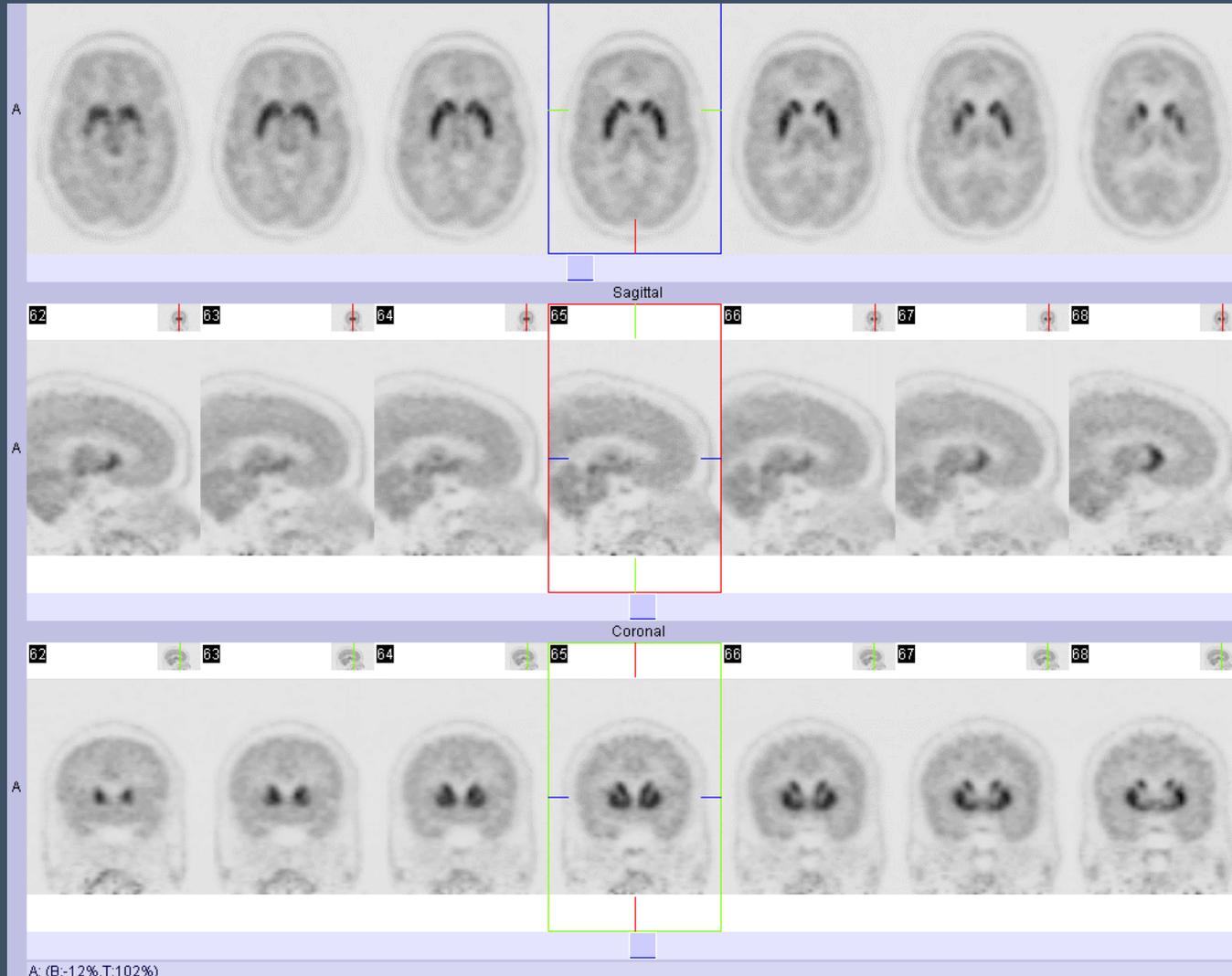


PS

# Asymmetric PD



# F18 AV 133 VMAT agent for PD



# Benefits of DaTScan

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- § Improves diagnosis in early PD
- § Distinguishes PSD from other sources of tremor
- § Can have a significant impact on patient management ( May change management in approximately 30%)
- § May save money on ineffective medications

# SPECT Cerebral Perfusion Imaging

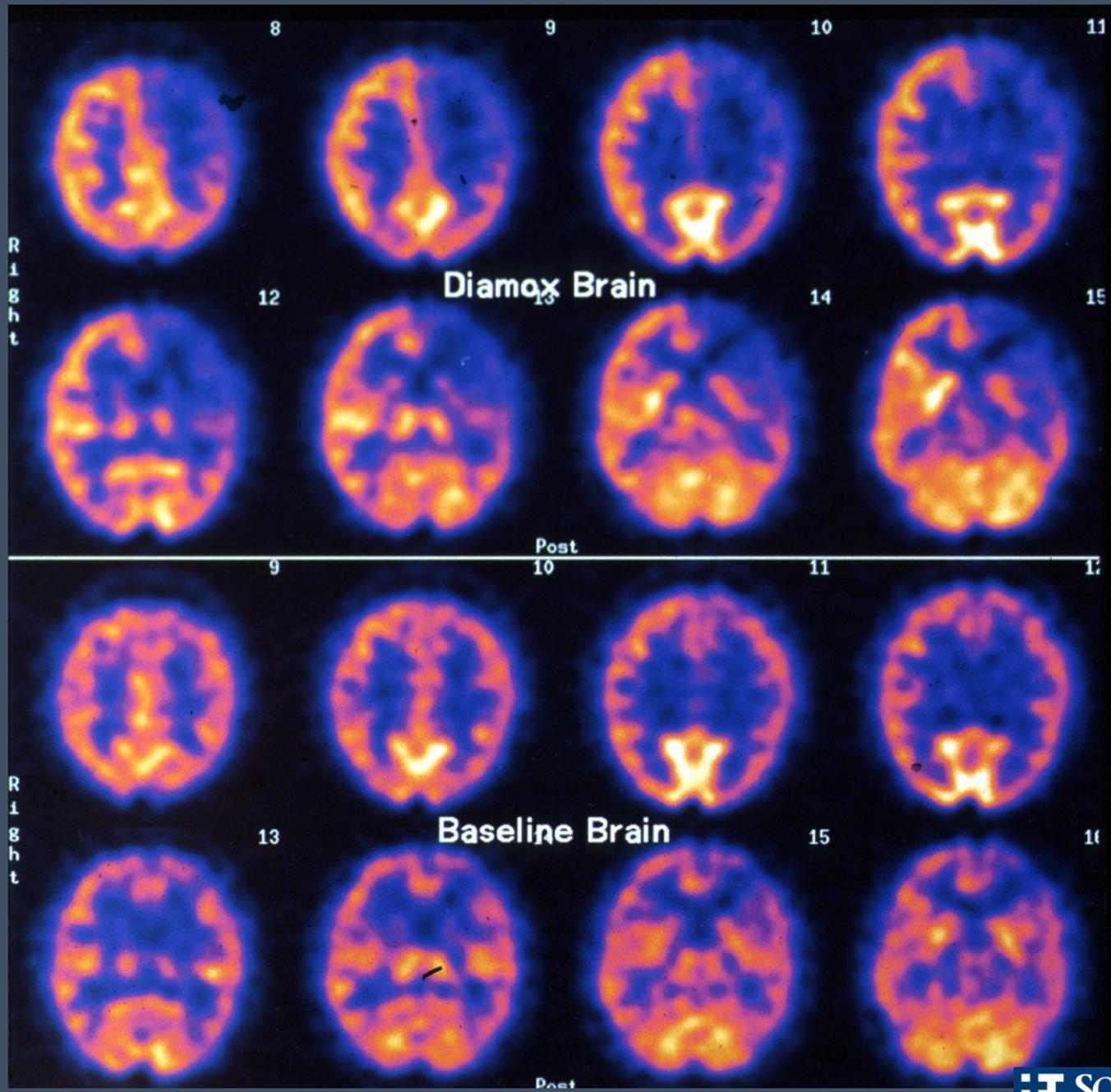
- § Vascular Reserve- Allows evaluation of cerebral perfusion in much the same way as cardiac perfusion imaging. By using acetazolamide as a vasodilator, areas of the brain that are already maximally vasodilated may be revealed, yielding information about the impact of arterial stenoses and occlusions
- § Trial Balloon Occlusion- Allows evaluation of the cerebral collateral circulation in response to temporary occlusion of a major cerebral artery
- § Dementia –Demonstrates perfusion patterns in demonstration which corresponds to brain areas of hypometabolism seen with PET FDG
- § Epilepsy-Allows evaluation of areas of potential abnormal perfusion associated with seizure foci in focal epilepsy
- § Other uses

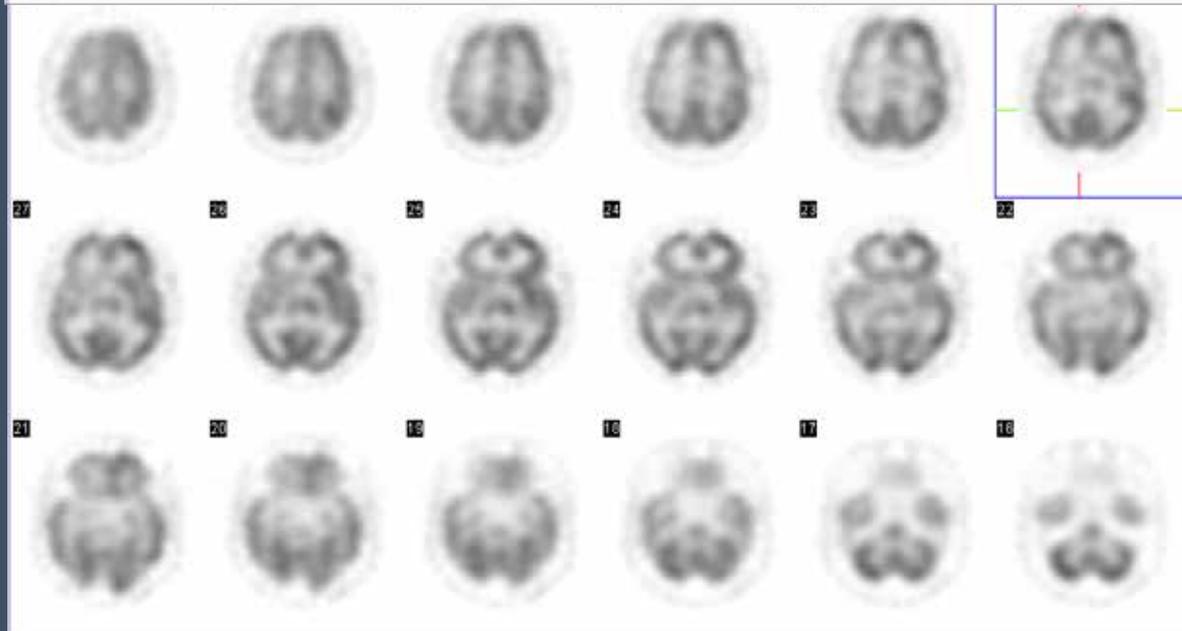
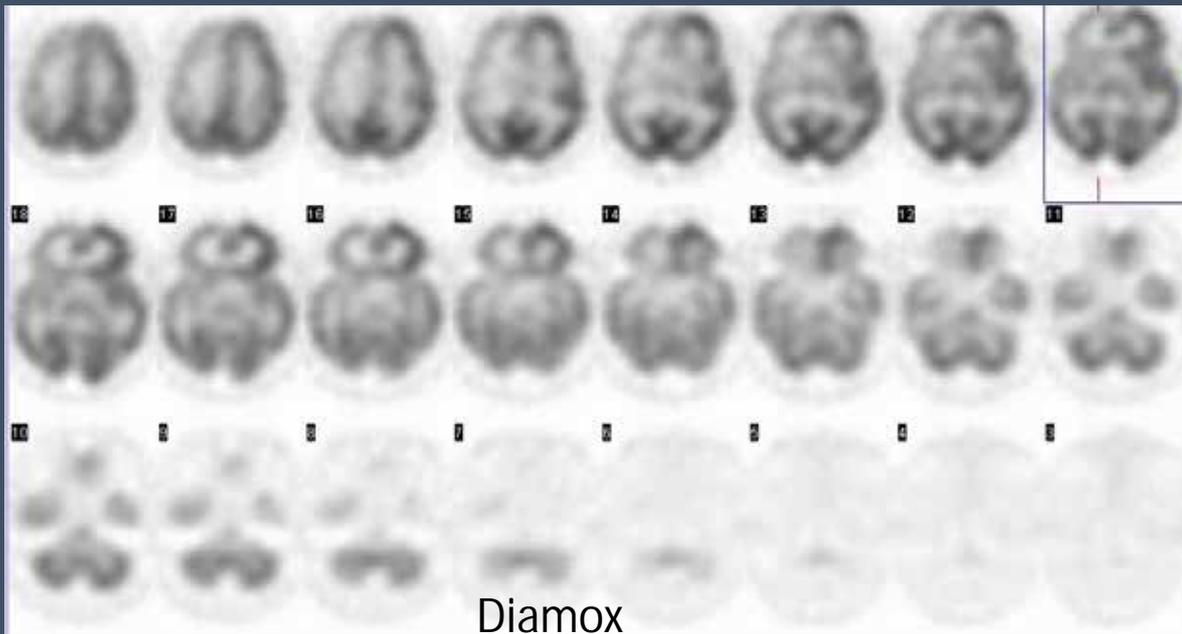
# SPECT Cerebral Perfusion Imaging

- § The CBF tracers commonly used for the purposes discussed in this lecture are Tc 99m ethylene cysteine dimer (ECD) and Tc 99m hexamethylpropyleneamine oxime (HMPAO)
- § Both tracers cross the blood brain barrier rapidly after injection and both are rapidly metabolized into a hydrophilic form that will not cross back through the blood brain barrier
- § Both are stabilized so that they can be injected several hours after preparation . This allows their use for capturing what may be a transient event, such as a temporary arterial occlusion or a seizure
- § Both may be imaged using SPECT or SPECT CT gamma cameras optimized for brain imaging

# Evaluation of Vascular Reserve

- § Patient injected with 1 g acetazolamide, a vasodilator. Patient then injected with perfusion tracer (usually Tc 99m ECD or HMPAO)
- § Brain SPECT Scan performed.
- § If areas of decreased perfusion seen
- § Baseline scan is performed on a different day.
- § Relative changes in perfusion distribution are indications of areas of reduced reserve
- § Areas of fixed reduction in perfusion usually indication of prior infarct which will not improve with reperfusion efforts.



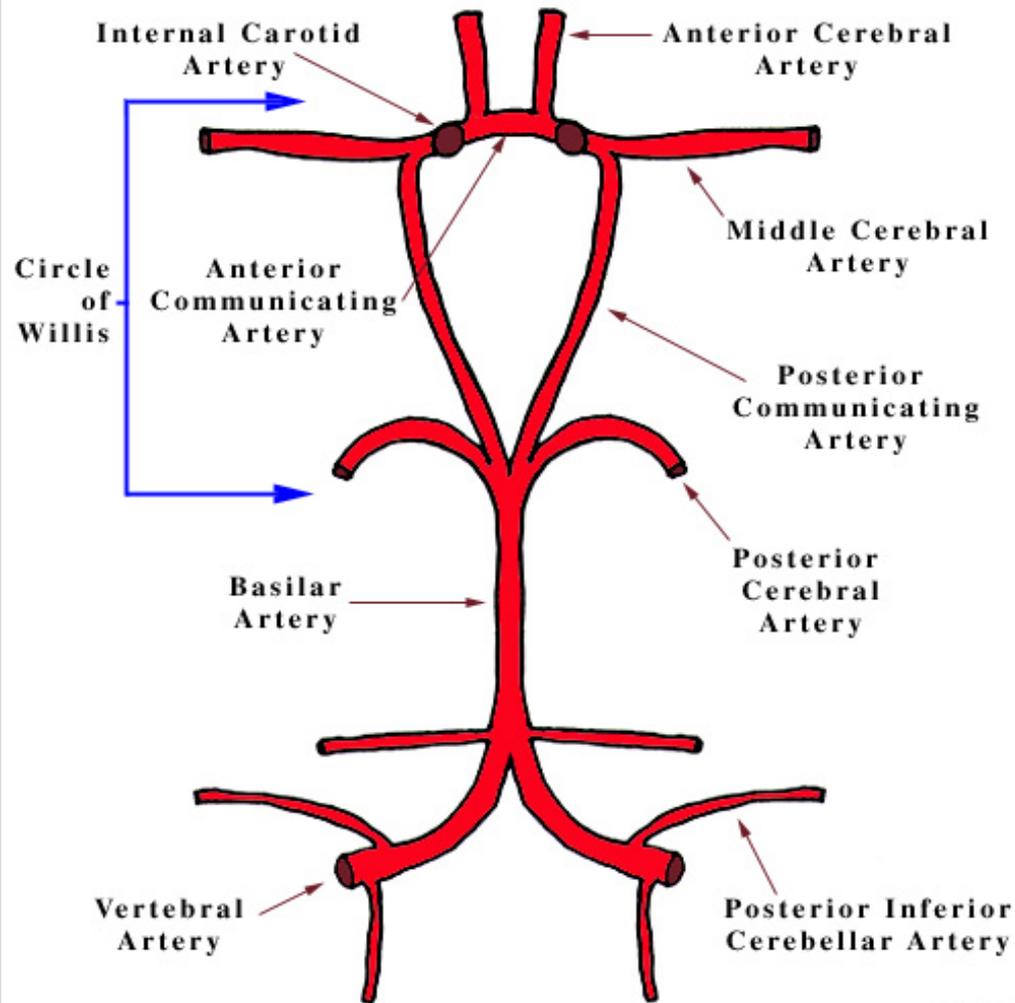


Baseline

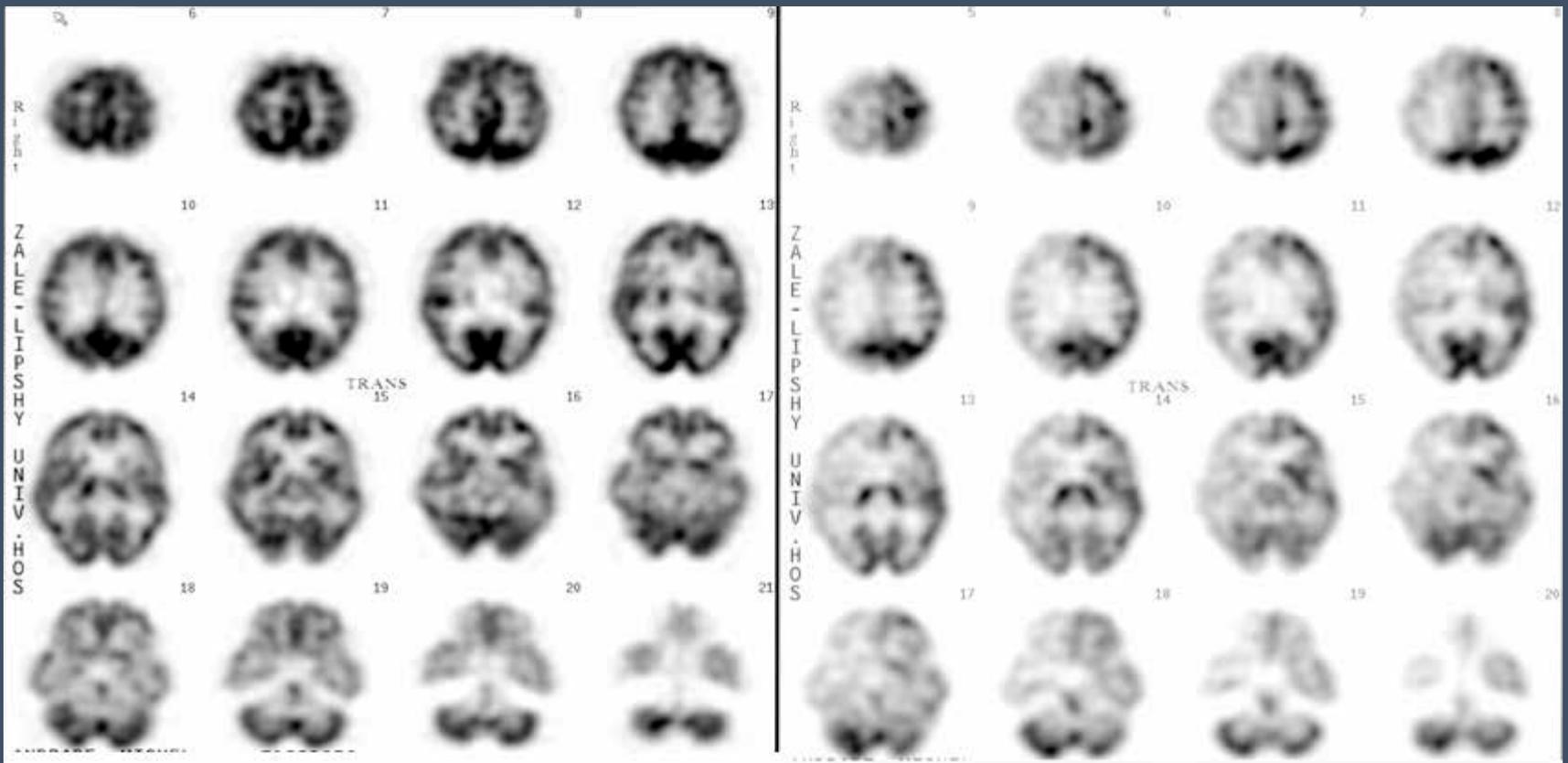
# Trial Balloon Occlusion

- § This refers to the temporary occlusion of a major cerebral artery usually the internal carotid artery. This is done to evaluate collateral blood flow in the event that the artery being evaluated needs temporary or permanent occlusion in order to treat an aneurysm in the brain or a tumor in the neck.
- § Angiographic catheter placed in vessel of interest
- § Balloon inflated, serial neurological exams and injection of tracer, while the balloon inflated. Inflation in the balloon maintained in the artery for approximately 15 minutes or until the patient becomes symptomatic (whew!!!)
- § Balloon deflated
- § SPECT scan performed

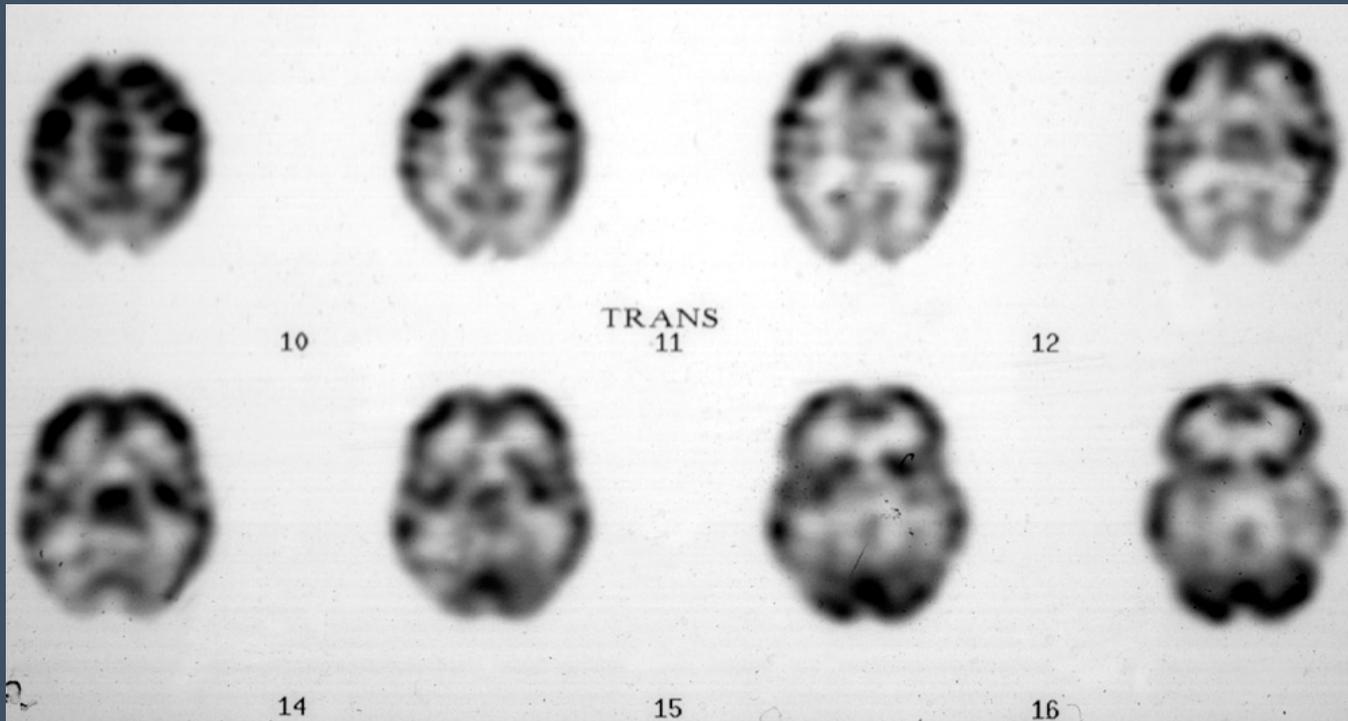
## CIRCLE OF WILLIS



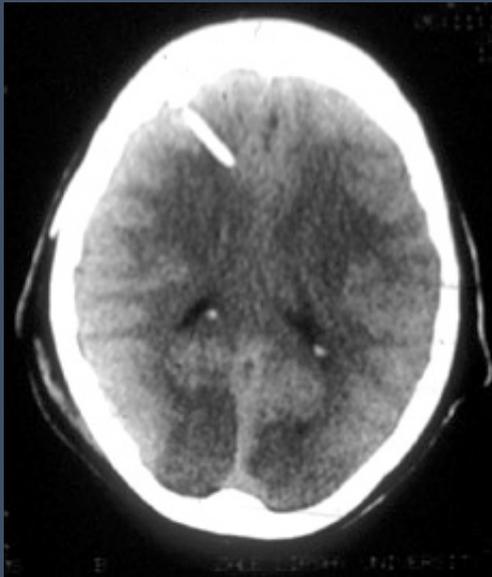
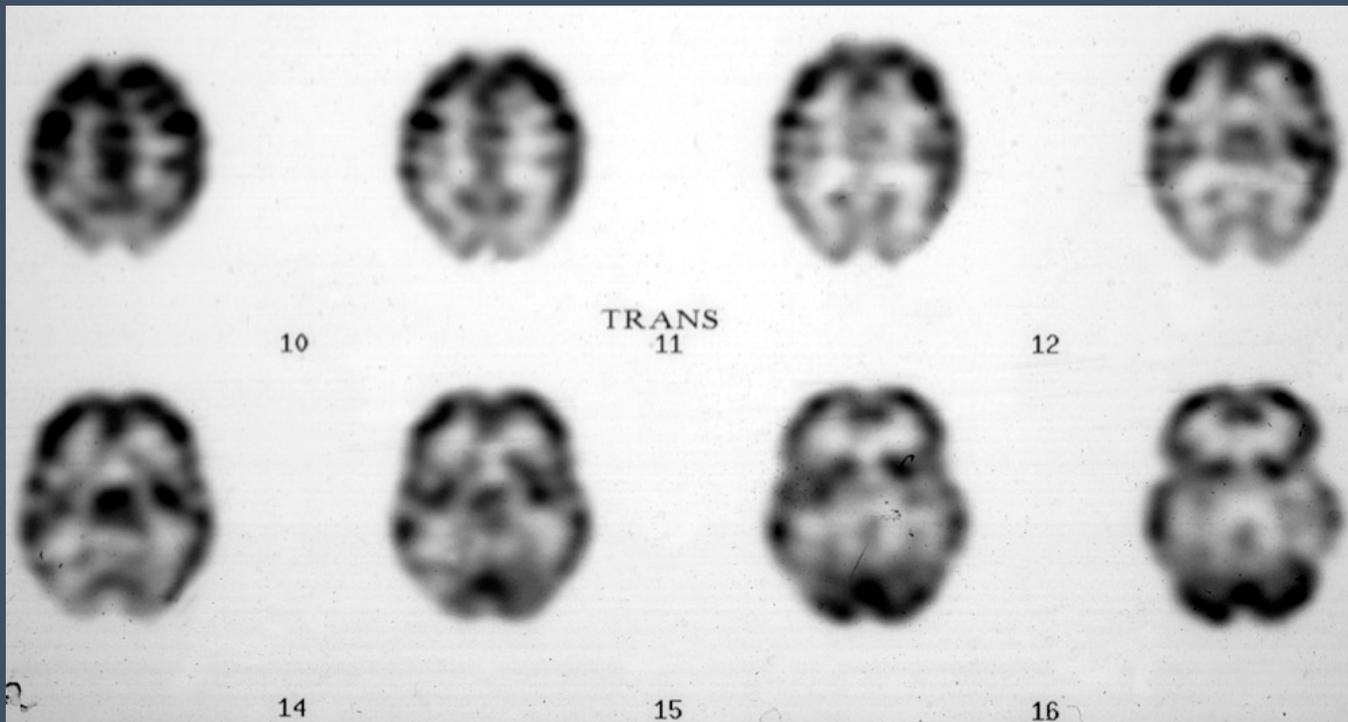
Complete Circle of Willis which occurs about 50% of the time



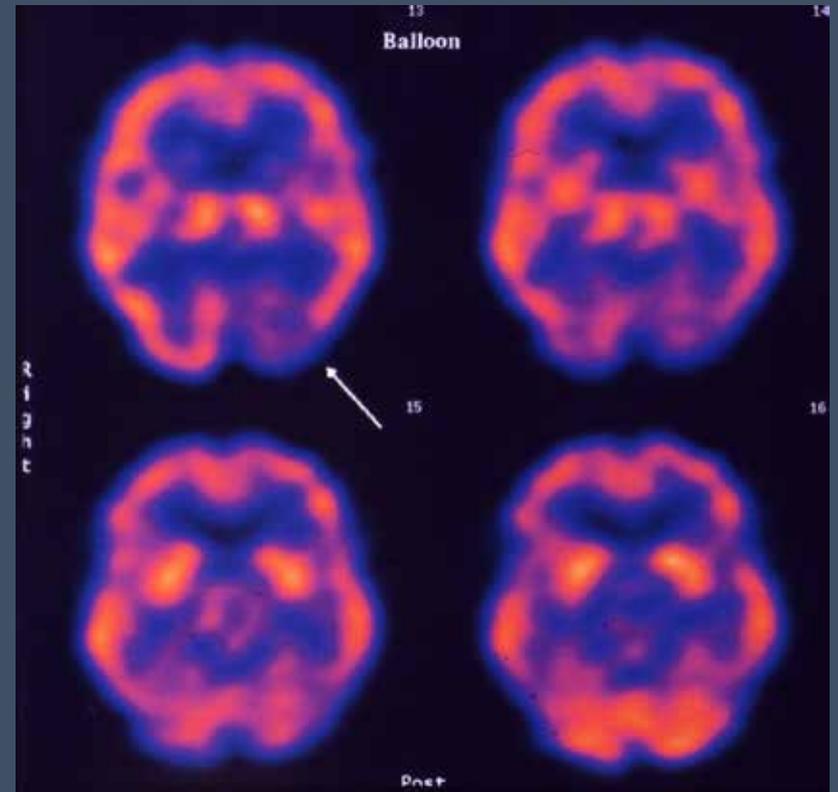
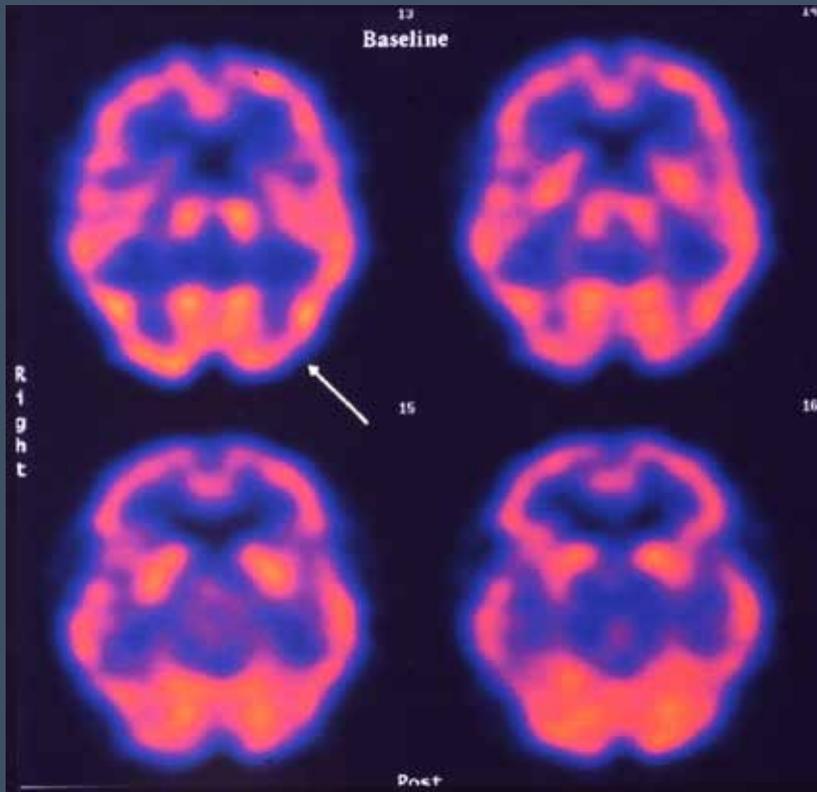
TBO of right ICA for patient with large thyroid cancer



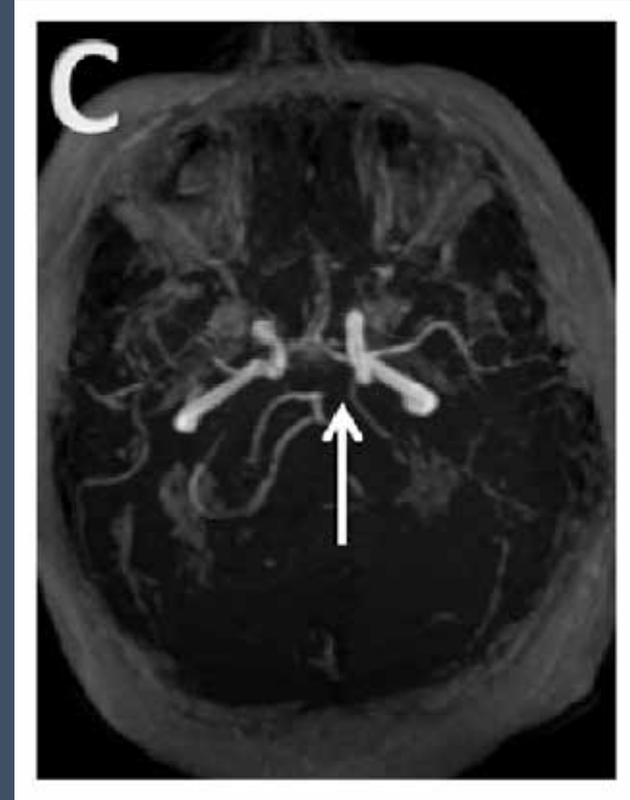
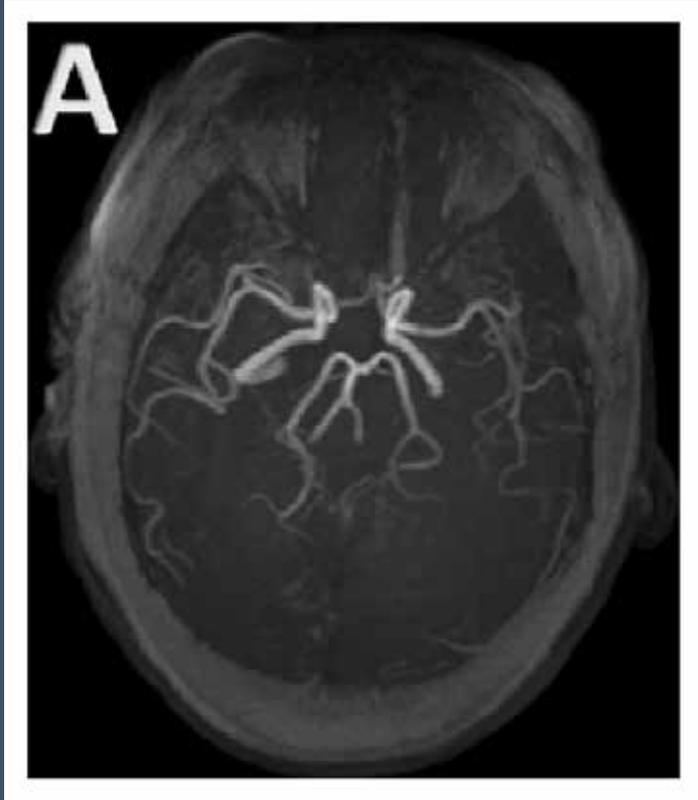
TBO of basilar artery in patient with BA stenosis,  
baseline normal



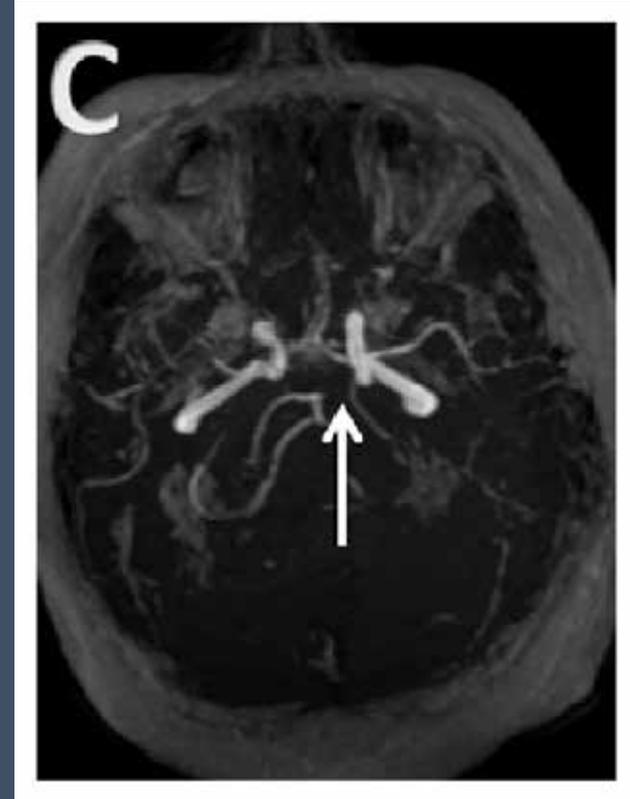
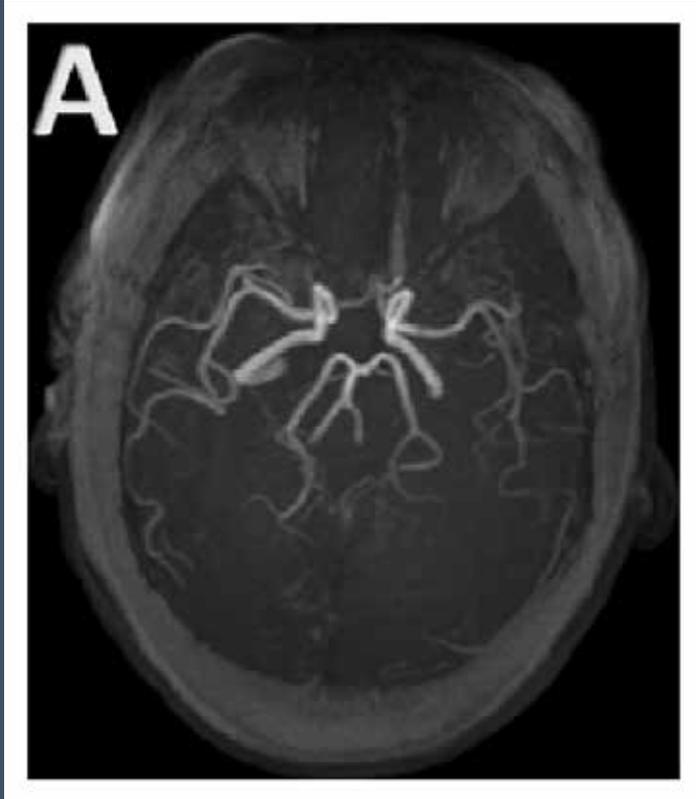
Attempts to dilate that stenosis  
did not go well



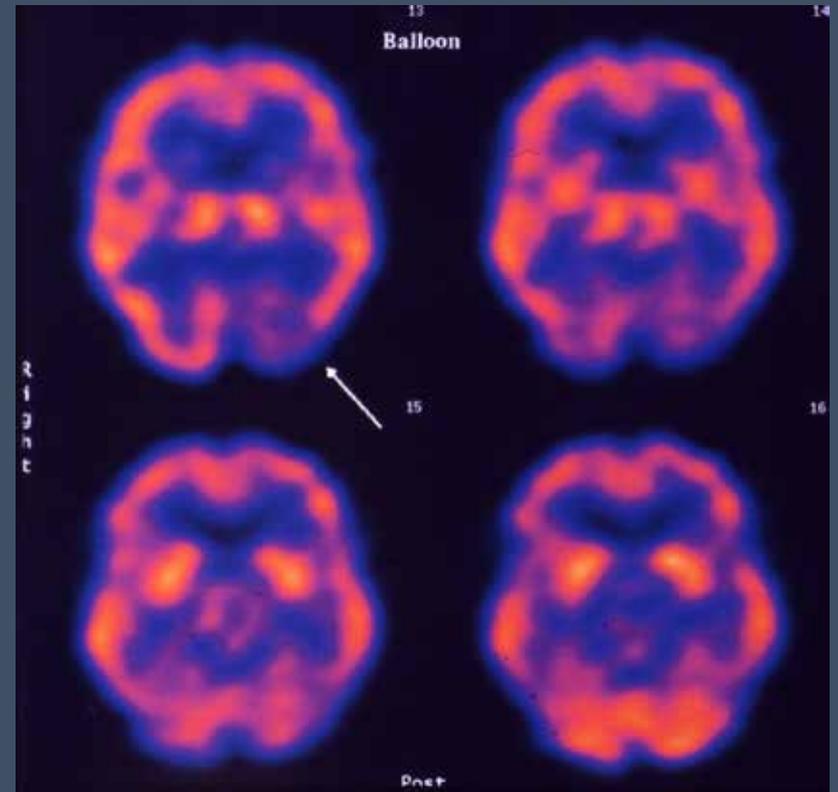
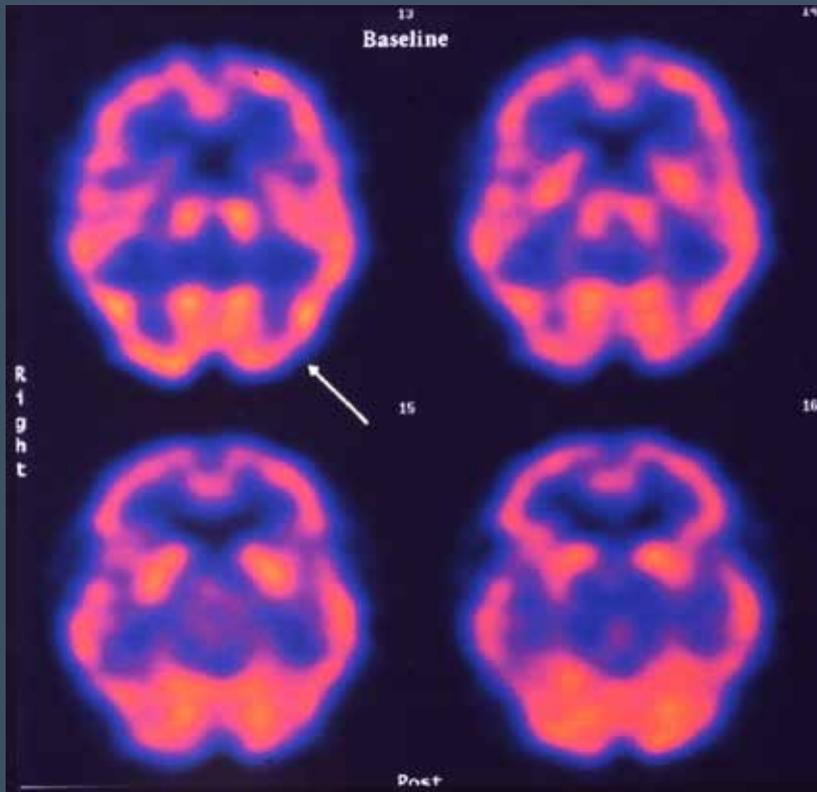
Patient undergoing left internal carotid TBO. What is the problem?



What is the arrow pointing to?



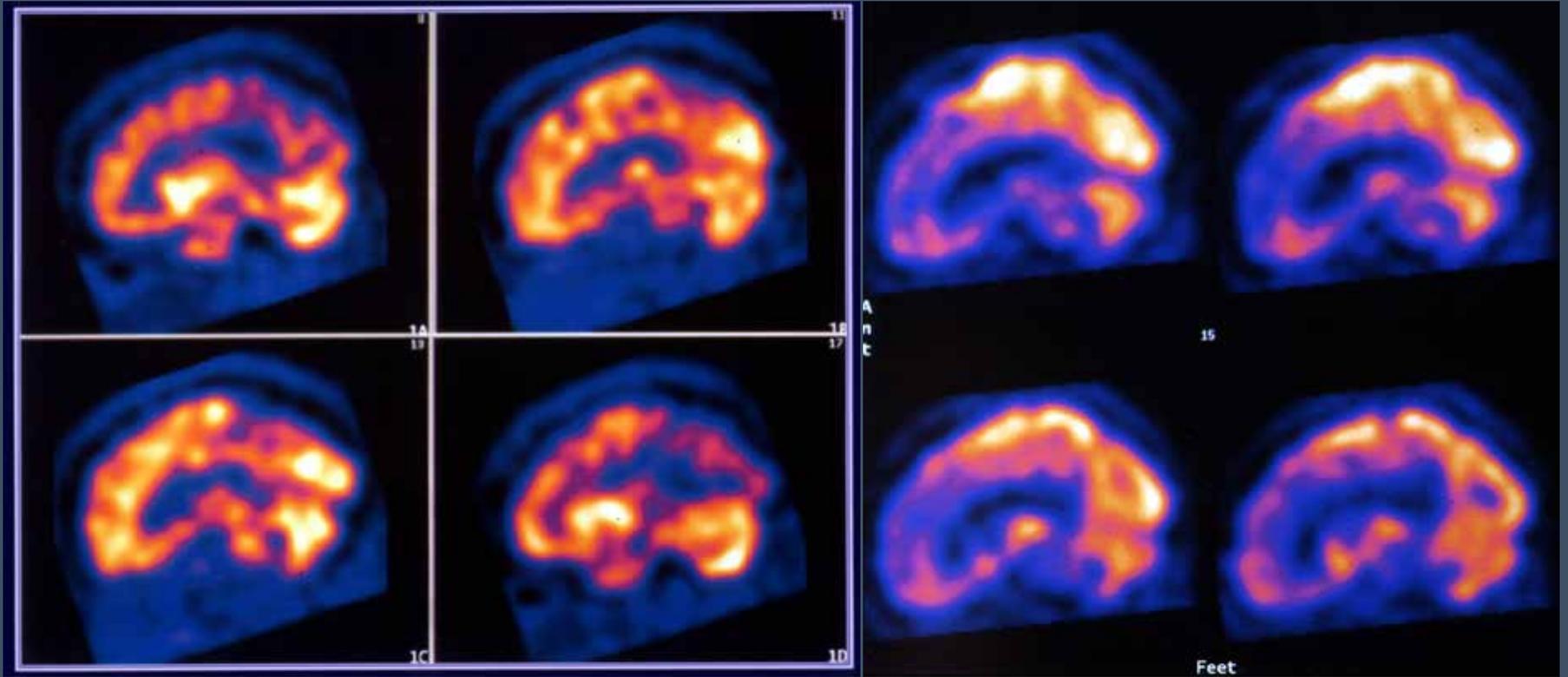
The arrow is pointing to the PCA which in this case is fetal in origin, meaning it arises from the ICA and not the BA



Patient undergoing left internal carotid TBO. What is the problem?

# SPECT CBF and FDG PET

- § SPECT CBF shows perfusion of brain tissue
- § FDG PET shows metabolism of brain tissue
- § Because there is tight coupling in the regulation of both blood flow and metabolism, these two scan types can often show the same patterns of abnormality in a brain area affected by a disease process
- § For example, prior to the widespread availability of FDG PET imaging, SPECT CBF was used to image a whole range of disease processes that are now mainly evaluated by brain FDG PET. These include dementia and epilepsy



SPECT CBF in ATD

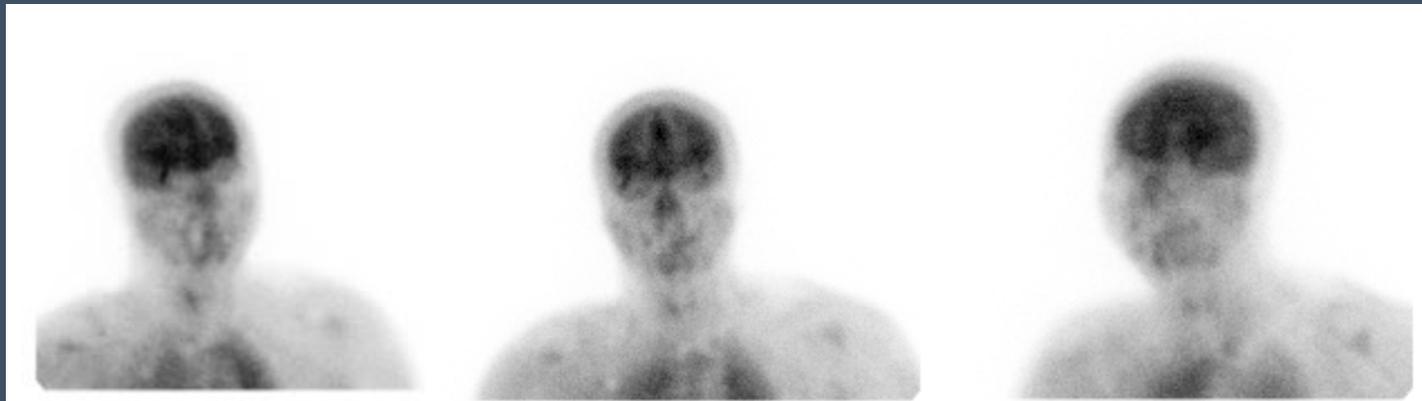
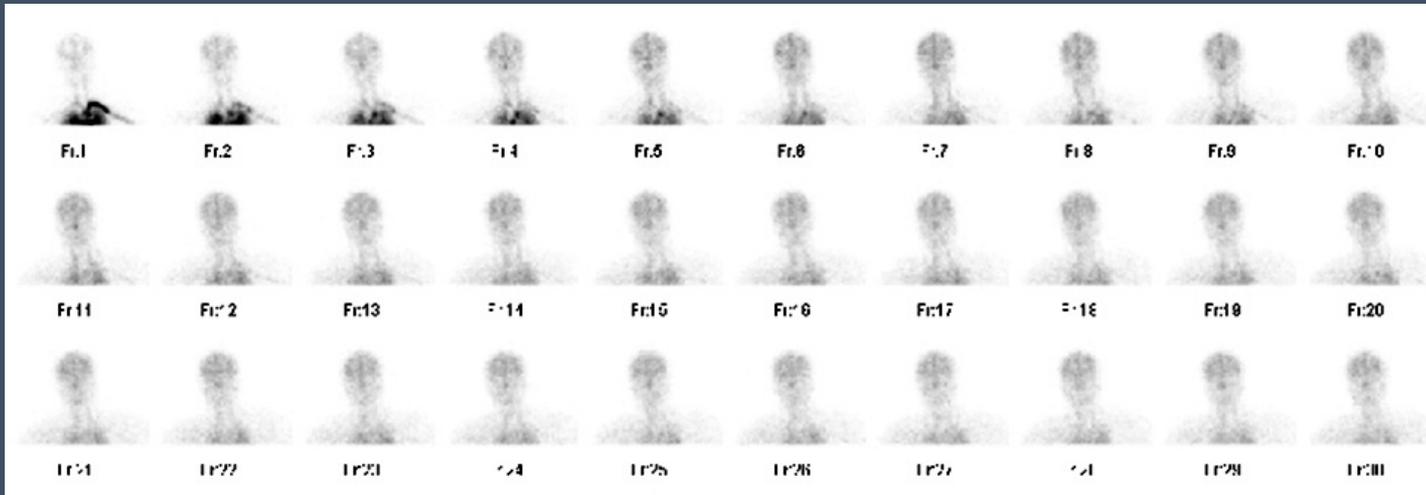
FTD

# Cerebral Perfusion Scanning in Brain Death

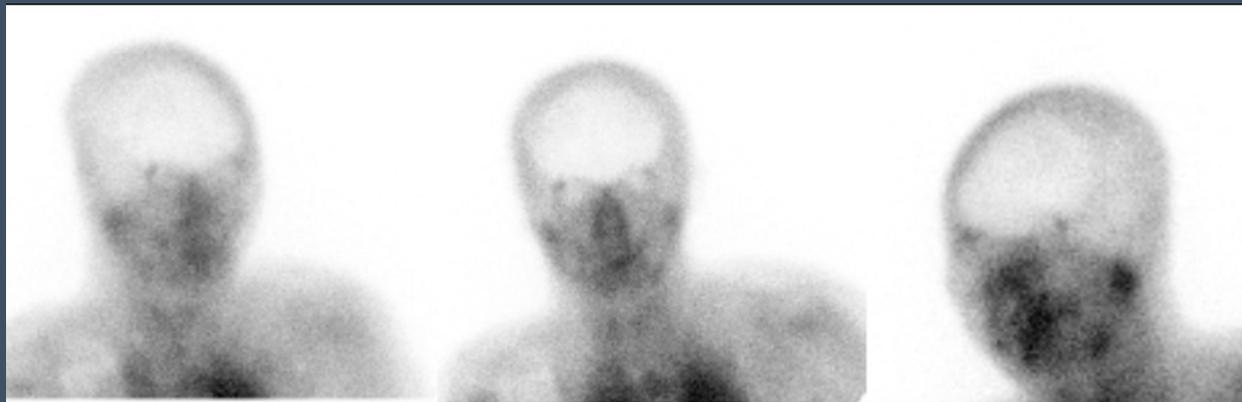
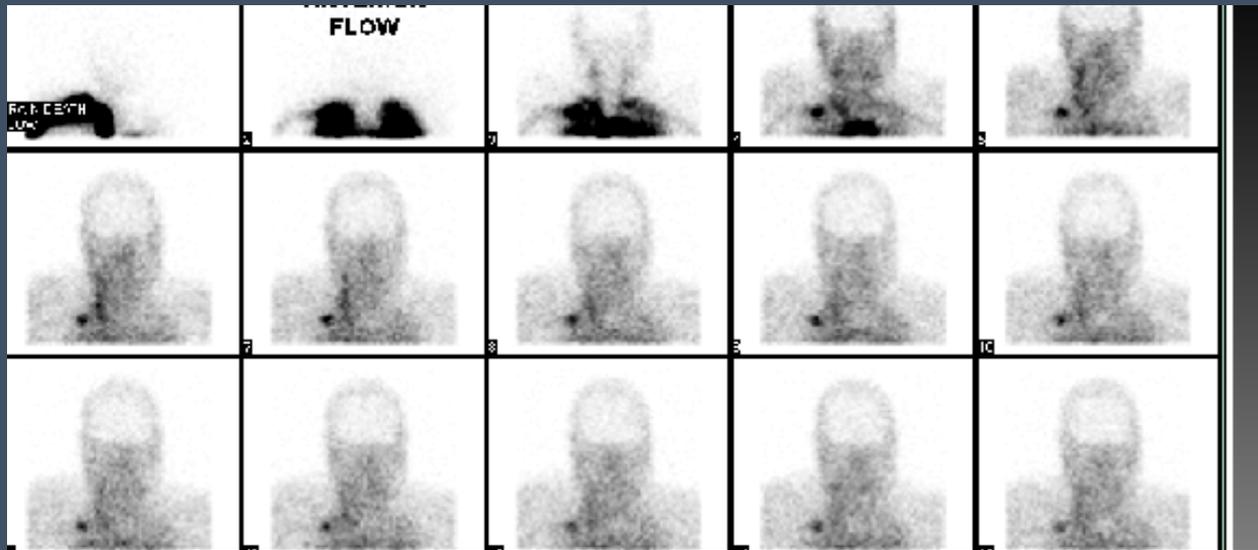
- § “Brain death” refers to cessation of all functions of the brain including the brain stem.
- § Brain death is determined by clinical examination of the patient for evidence of lack of brainstem functions
- § At times, there is desire to have additional “confirmatory” evidence of brain death. This may include obtaining an electrical encephalogram (EEG) or a scan to confirm lack of intracerebral perfusion
- § When the brain is irreversibly damage through either direct trauma or anoxic injury, swelling occurs which eventually raises intracerebral pressure to the point where arterial brain perfusion no longer occurs

# Cerebral Perfusion Imaging in Brain Death

- § Can be done using Tc 99m DTPA.
  - § Benefits-can be repeated in a short period of time
  - § Drawbacks-captures only arterial phase and may be difficult to interpret for less experienced readers
- § Can be done using Tc 99m HMPAO or ECD
  - § Benefits-easier to interpret on the delayed images
  - § Drawbacks- Not repeatable until about 24 hours



Intracerebral perfusion remains



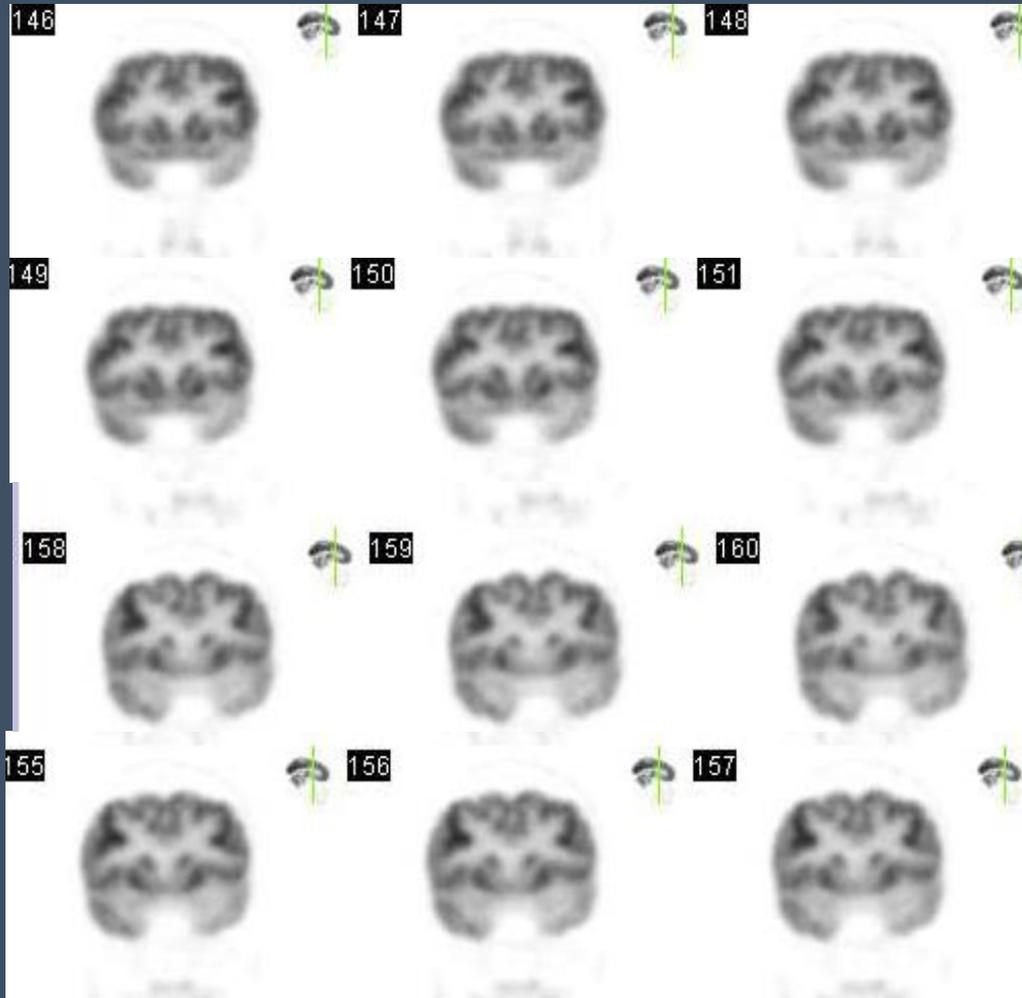
Intracerebral perfusion absent

# SPECT and PET Imaging in Epilepsy

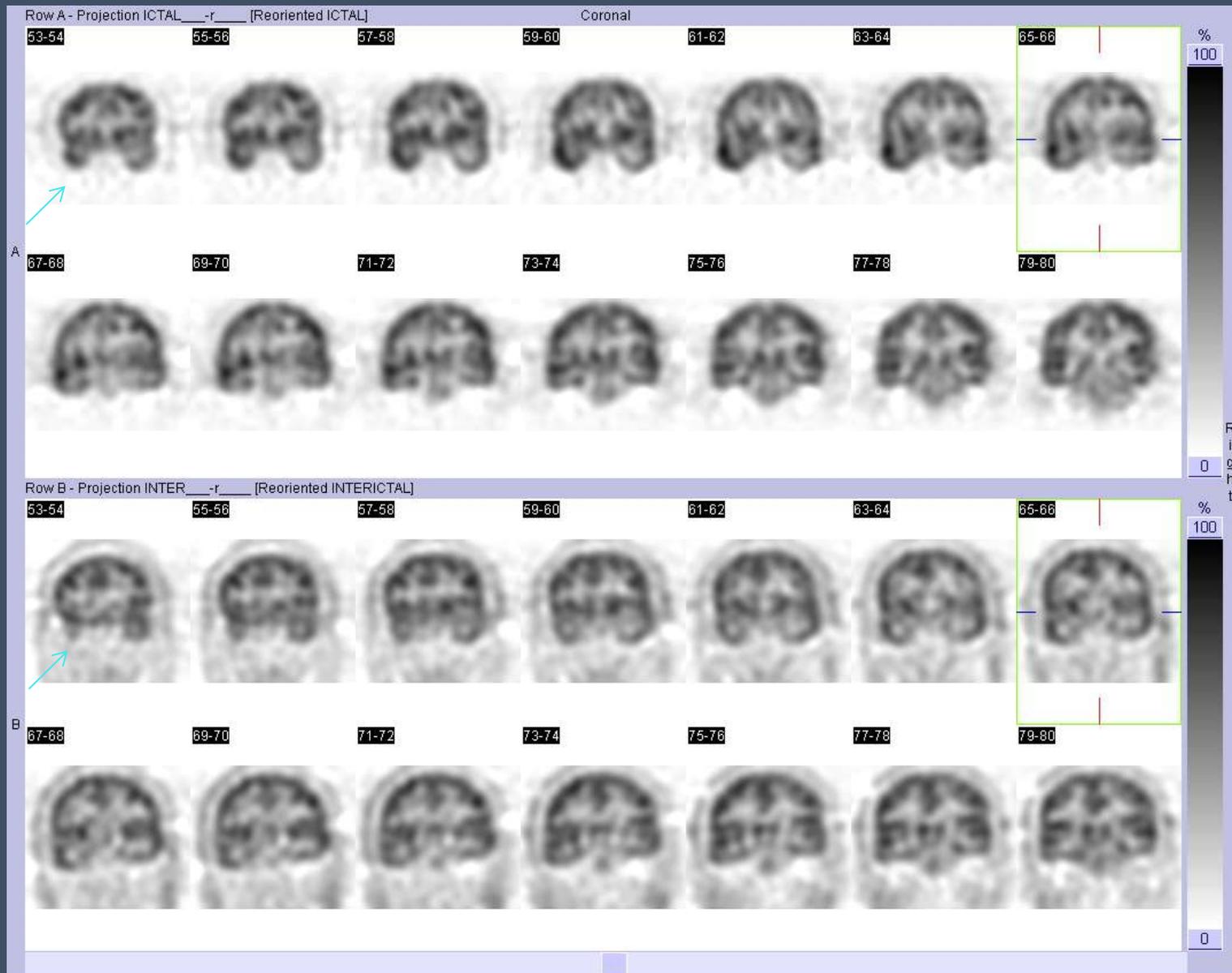
- § About 50/10,000 new cases of epilepsy each year. About 1/3 of these patients are not controlled by antiepileptic drugs (AED).
- § About half of these patients will develop focal epilepsy, most commonly involving the temporal lobes. Some of these patients may benefit significantly from temporal lobectomy
- § MRI is very important in identifying structural lesions which may be epileptogenic. These most commonly are hippocampal sclerosis, but other causes include cortical dysplasia and mass lesions such as tumors, cavernomas, arteriovenous malformations, etc
- § However, about 15-30% of patients with intractable focal epilepsy have no identifiable structural lesions
- § These are the patients where SPECT CBF and FDG PET may be very beneficial in identifying the seizure focus

# SPECT and PET Imaging in Epilepsy

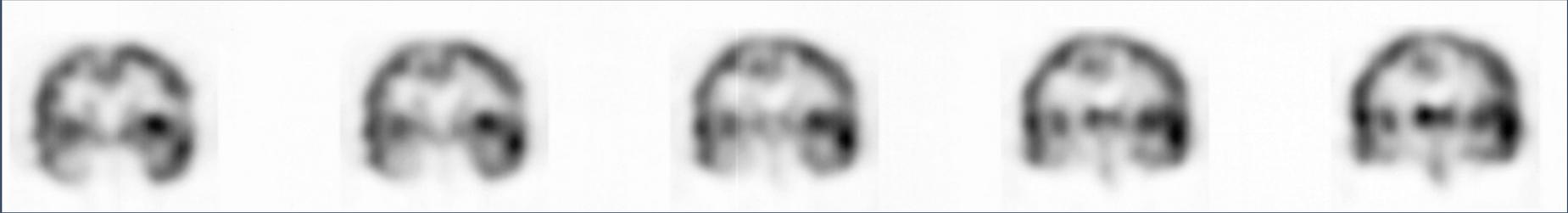
- § Between seizures, the blood flow and metabolism of the brain area surrounding the seizure focus may be reduced, indicating poor function of these areas.
- § During seizures, the blood flow and metabolism in these areas may be increased. However this increase is very transient so for optimal evaluation, the patient has to be injected with tracer during a seizure.
- § When an ictal (during seizure) and interictal (between seizures) scans are compared, the changes in blood flow and metabolism help identify the regions of concern.



Patient with left temporal lobe cavernoma and Interictal PET showing hypo metabolism in left temporal lobe



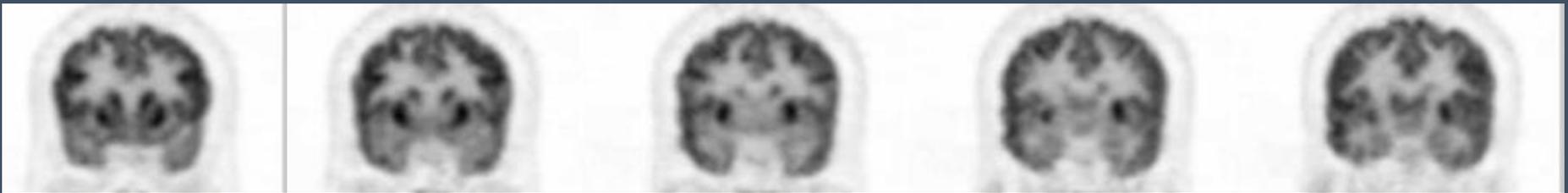
SPECT CBF in epilepsy identifying perfusion changes between the right temporal lobe between and during seizures



Ictal SPECT



Interictal SPECT



Interictal PET

# Other PET Tracers Used in Imaging Epileptogenic Foci

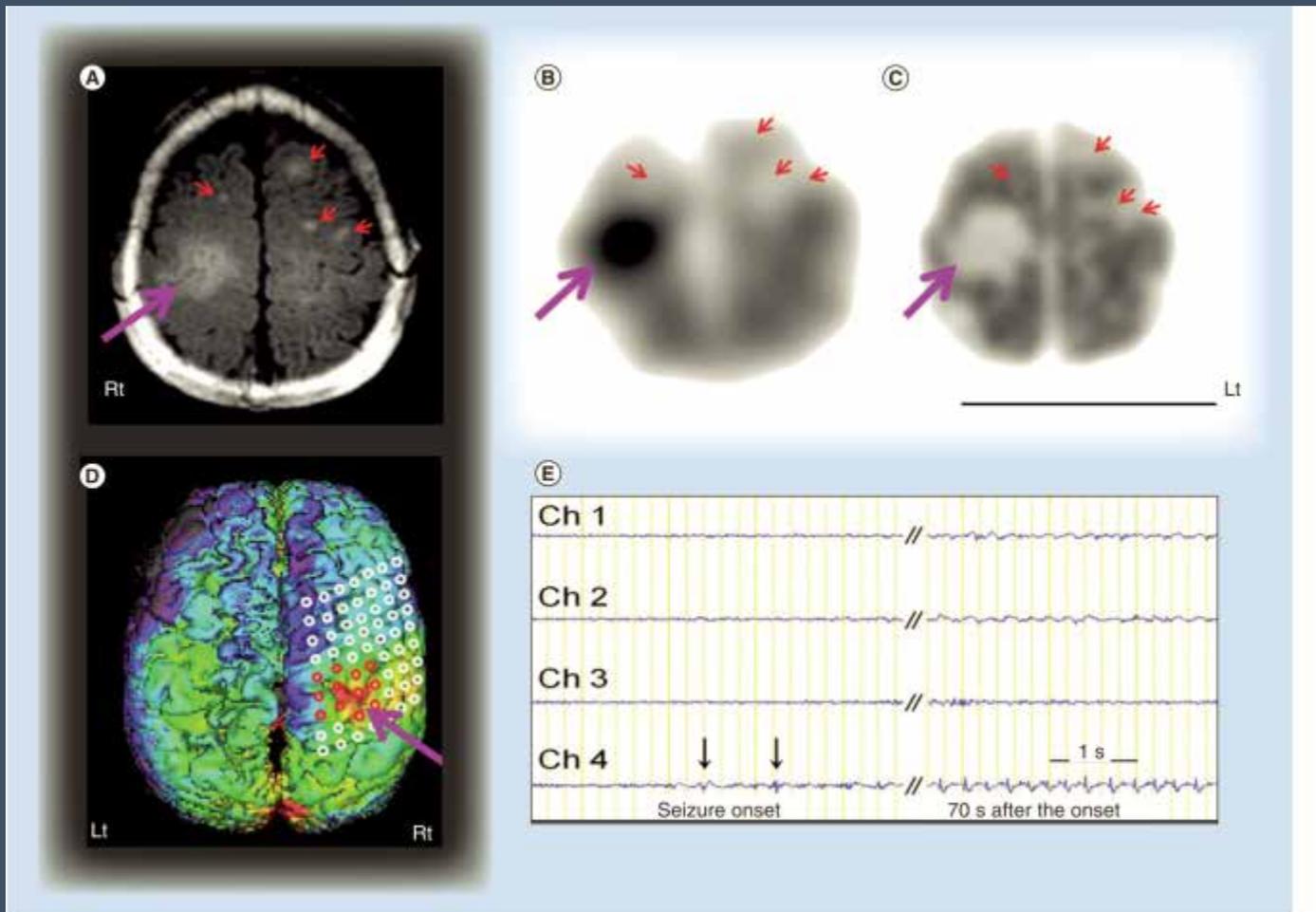
**Table 1**

Mechanism of uptake/binding pattern of various PET tracers in epileptogenic foci.

PET tracer	Mechanism/target	Uptake/binding pattern in epileptogenic foci
FDG	Glucose metabolism	Interictal decrease Ictal increase
<sup>15</sup> O-H <sub>2</sub> O (water)	Blood flow	Interictal decrease Ictal increase
AMT	Tryptophan metabolism to serotonin or quinolinic acid	Interictal increase <sup>†</sup>
FMZ	GABA <sub>A</sub> /benzodiazepine receptor (antagonist)	Interictal decrease
<sup>11</sup> C-PK11195	Peripheral benzodiazepine receptor (antagonist)	Increased
<sup>11</sup> C-(S)-[N-methyl]-ketamine	NMDA receptor (antagonist)	Decreased
<sup>11</sup> C- <i>l</i> -deprenyl	MAO-B (inhibitor)	Increased
<sup>11</sup> C-doxepin	H <sub>1</sub> receptor (antagonist)	Increased
<sup>11</sup> C/ <sup>18</sup> F-FCWAY	5HT <sub>1A</sub> receptor (antagonist)	Decreased
<sup>18</sup> F-MPPF	5HT <sub>1A</sub> receptor (antagonist)	Decreased
<sup>18</sup> F-altanserin	5HT <sub>2A</sub> receptor (antagonist)	Decreased
<sup>11</sup> C-carfentanyl	μ-opioid receptor (agonist)	Increased
<sup>11</sup> C-methylnaltrindole	δ-opioid receptor (antagonist)	Increased
<sup>18</sup> F-cyclofoxy	μ,κ-opioid receptor (antagonist)	Increased
<sup>11</sup> C-diprenorphine	μ,δ,κ-opioid receptor (antagonist)	Decreased
<sup>11</sup> C-NMPB	mACh receptor (antagonist)	Decreased
<sup>123</sup> I-iododexetimide	mACh receptor (antagonist)	Decreased

<sup>†</sup>AMT is the only tracer that can delineate and identify the 'epileptic focus' in the 'interictal' state in patients with tuberous sclerosis.

Ach: Acetylcholine; AMT: <sup>11</sup>C-*l*-tryptophan; FCWAY: Trans-4-fluoro-*N*-2-[4-(2-methoxyphenyl) piperazin-1-yl] ethyl-*N*-(2-pyridyl) cyclohexanecarboxamide; FDG: 2-<sup>18</sup>F-fluoro-2-deoxy-*D*-glucose; FMZ: <sup>11</sup>C-flumazenil; H: Histamine; HT: Hydroxytryptamine; MAO-B: Monoamine oxidase-B; MPPF: 4-(2-methoxyphenyl)-1-[2-(*N*-2"-pyridinyl)-*p*-fluorobenzamido] ethylpiperazine; NMDA: *N*-methyl-*D*-aspartic acid; NMPB: 4-*N*-methylpiperidinyll benzilate; PK11195: 1-(2-chlorophenyl)-*N*-methyl-*N*-(1-methylpropyl)-3-isoquinoline carboxamide.



**Figure 1. Usefulness of  $\alpha$ -methyl-L-tryptophan PET in tuberous sclerosis patients with nonlateralizing EEG**

A. MRI, B. PET with AMT, C. PET with FDG, D. Intracranial electrode Location, E. EEG in patient with TS

# CME Questions

1. DATScan imaging is likely to be abnormal in patients with
  - § Tremor of Cerebellar origin
  - § Drug induced parkinsonian tremor
  - § Parkinson's Disease
  - § Essential Tremor

# CME Questions

1. DATScan imaging is likely to be abnormal in patients with
  - § Tremor of Cerebellar origin
  - § Drug induced parkinsonian tremor
  - § Parkinson's Disease
  - § Essential Tremor
  - § References 1-2

# CME Questions

2. Syndromes involving loss of CNS dopamine may include

- § a. Parkinson's Disease
- § b. Progressive Supranuclear Palsy
- § c. Multisystem atrophy
- § d. All may result from loss of dopamine

# CME Questions

2. Syndromes involving loss of CNS dopamine may include

§ a. Parkinson's Disease

§ b. Progressive Supranuclear Palsy

§ c. Multisystem atrophy

§ d. All may result from loss of dopamine

§ References 1-2

# CME Questions

3. SPECT CBF can be used to evaluate

§ a. Vascular reserve

§ b. Cerebral collateral perfusion

§ c. Epilepsy

§ d. CBF can evaluate all of the above

§ References 3 and 5

# CME Questions

3. SPECT CBF can be used to evaluate

§ a. Vascular reserve

§ b. Cerebral collateral perfusion

§ c. Epilepsy

§ d. CBF can evaluate all of the above

§ References 1-4

# CME Questions

4. In evaluating epilepsy, the time when increased CBF at the seizure focus is most likely to be visualized is

- § a. During a seizure
- § b. Just after a seizure
- § c. Between seizures
- § d. Anytime

# CME Questions

4. In evaluating epilepsy, the time when increased CBF at the seizure focus is most likely to be visualized is

- § a. During a seizure
- § b. Just after a seizure
- § c. Between seizures
- § d. Anytime
- § Reference 4

# CME Questions

5. Cerebral blood flow imaging of the brain and FDG PET imaging of the brain often show similar findings in dementia and epilepsy because

- § a. They are showing the same process
- § b. There is tight coupling between brain blood flow and brain metabolism
- § c. They both measure brain oxygenation
- § d. They don't have anything to do with each other

# CME Questions

5. Cerebral blood flow imaging of the brain and FDG PET imaging of the brain often show similar findings in dementia and epilepsy because

- § a. They are showing the same process
- § b. There is tight coupling between brain blood flow and brain metabolism
- § c. They both measure brain oxygenation
- § d. They don't have anything to do with each other
- § Reference 4

# References

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