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Department of Radiology

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Didactic

Diamox Brain SPECT

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3 approaches can be used in the evaluation of patients with cerebrovascular disease:

1. measurement of the cerebral blood volume (CBV) /cerebral blood flow ratio, mathematically equivalent to the mean transit time (MTT)
2. degree of cerebral flow reserve; comparing CBF under baseline conditions and after a vasodilator stimulus such as ACZ
3. direct measurements of OEF to identify patients with increased oxygen extraction (currently performed by using positron-emission tomography [PET])

- clinical value of resting rCBF is of questionable significance in the assessment of cerebrovascular disease, due to a strong coupling of flow and metabolism within the brain.
- regions of decreased flow do not necessarily indicate a primary vascular supply problem, but may be seen in areas of decreased metabolic demand-deafferentation (diaschisis), selective neuronal loss and chronic ischemia.
- normal CBF at rest need not indicate an adequate vascular supply since local vasodilation may exist distal to vascular compromise. Such areas should potentially, however, have a decreased vascular reserve.

Assessment of cerebral vascular reserve

- assess the circulation at rest and after a vasodilatory stimulus (stress) to access flow reserve
- Areas of decreased flow reserve should not manifest an increase in vascular flow to the same extent as regions of normal vascular supply
- Areas of loss of selective neurons or deafferentation have normal vascular supply and although they have decreased rCBF at rest they should respond normally after a vasodilatory stimulus
- evaluation of rest along with stress images, increase the specificity for the detection of cerebral vascular disease of rest-stress imaging over rest alone

Assessment of cerebral vascular reserve

- The vascular response of the brain is very sensitive to the CO_2 level with hypercapnia inducing vasodilation and an associated increase rCBF while flow is decreased with hyperventilation and resultant hypocapnia and alkalosis.
- Hypercapnia sufficient to induce flow changes that are measurable by PET or SPECT can be induced by breathing an enriched gas mixture containing 5% to 7% CO_2 .
- A more convenient and less cumbersome method of inducing vasodilatation than CO 2 inhalation is by the IV administration of acetazolamide (Diamox).

ACZ- mechanism of action

- Acetazolamide is a carbonic anhydrase inhibitor that causes an increase in CO_2 in red blood cells, brain parenchyma, or cerebral vasculature.
- direct effect of ACZ, independent of carbonic anhydrase inhibition, on the smooth muscle of the cerebral vasculature is another possible mechanism.

- rapid onset of vasodilation with maximal response at approximately 25 minutes and a half-time of 90 minutes.
- The dosage administered ranges from 500 to 1000 mg with the 1-g dose being most common. No additional increase in rCBF has been noted when increasing the ACZ dosage from 1 to 2 g.

Contraindications

- cardiovascular instability
- renal or hepatic insufficiency
- history of allergy to sulfa drugs

The use of vasodilators in patients with acute strokes should be approached with caution

Adverse effects (generally self-limited)

Side effects - occur in about 50% of patients & last for about 15 minutes

- a) numbness around mouth or fingers
- b) lightheadedness or blurred vision
- c) flushed feeling around face and neck
- d)Mild vertigo, tinnitus, paresthesias
- e) Nausea

- Reversible pontine ischemia caused by ACZ challenge has been discussed in a case report
- no acute ischemic sequelae in more than 1000 studies with the use of ACZ (Piepgras et al)

rCBF response to ACZ

- range of increase of rCBF of 5% to 70% , usually 30-50%
- response to ACZ has been described as independent of baseline flow and inversely related to age with decreasing response associated with increasing age.

- a decrease of 10 to 20% in activity on the Diamox exam compared to baseline is considered abnormal.

Dosage:

- Adults 1000 mg by slow iv push for typical patient.
- Children 14 mg/kg.

Protocol

- An I.V. line should be started 15-20 minutes before the tracer is administered.
- Patients should be injected with their eyes open and their ears unplugged (blood flow is increased by 30% in the occipital lobes when the eyes are open compared to closed).
- Inject 1 gm of acetazolamide intravenously over 5 minutes slowly.
- Check blood pressure and monitor blood pressure for 25 minutes.
- Wait 25 minutes and then inject the radiopharmaceutical.
- Wait 30 minutes (Tc99m-HMPAO or Tc99m-ECD) and acquire images in the usual manner.

- A baseline brain perfusion study without acetazolamide may be performed after a 1 day delay.
- exam has also been performed using both Tc99m-HMPAO and I-123 IMP

Limitations of the Diamox test

- Due to the nonlinear uptake properties of HMPAO and ECD, which underestimate perfusion in regions of increased flow, there can be limited contrast for flow differentiation.
- acetazolamide has been shown to increase cerebral blood flow by only about 30% to 50% above baseline in normal older patients (range 5 to 70%). This is in contrast to coronary pharmacologic stress examinations in which coronary blood flow is increased by 300-400%.

Cerebral perfusion agents

(lipophilic agents that are transported from the arterial vascular compartment to the normal brain tissue compartment by diffusion and distributed proportional to rCBF)

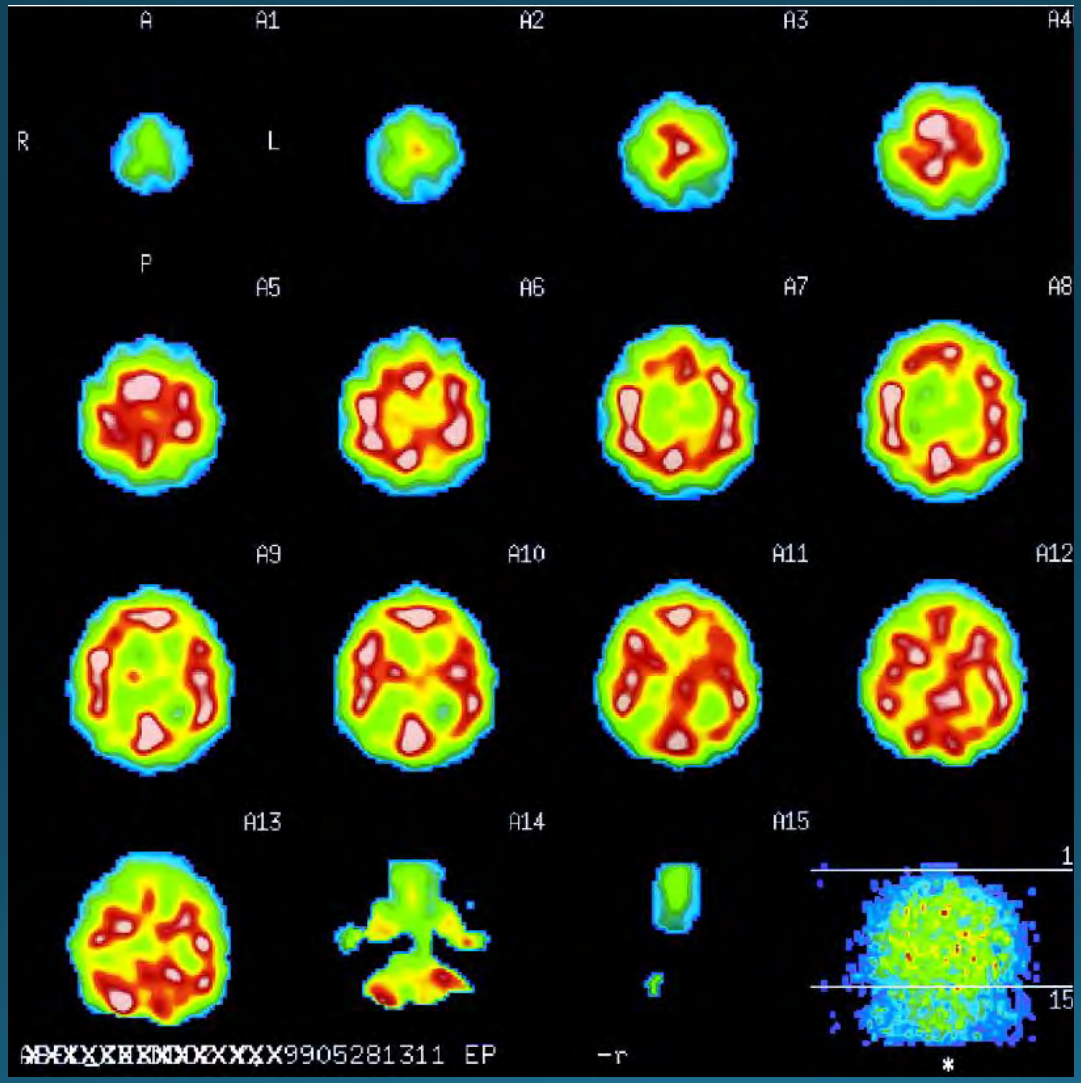
- Tc99m-HMPAO and Tc99m-ECD T99m-labelled tracers are essentially irreversibly trapped in the tissue compartment
- Xe 133- freely diffusible not trapped in tissue (used in determination of clearance rate)
- I123-IMP unique properties of redistribution can be used in low flow state.

133-Xenon

- T1/2: 126 hours
- Low-energy gamma rays: 81 keV
- intra-arterial, intravenous, or by inhalation routes
- inert, lipid soluble gas which does not undergo any chemical transformation in the brain
- the best agent for determination of absolute quantitative blood flow (rCBF in mL/min/100 gm tissue)
- by measuring cerebral washout of the inhaled gas, an absolute rCBF can be obtained (washout is directly proportional to blood flow)

- Clinical use is limited:

1. rapid transit and short biologic half-life in the brain
2. low gamma energy of Xe-133 results in marked attenuation of deep structures which results in less than optimal SPECT images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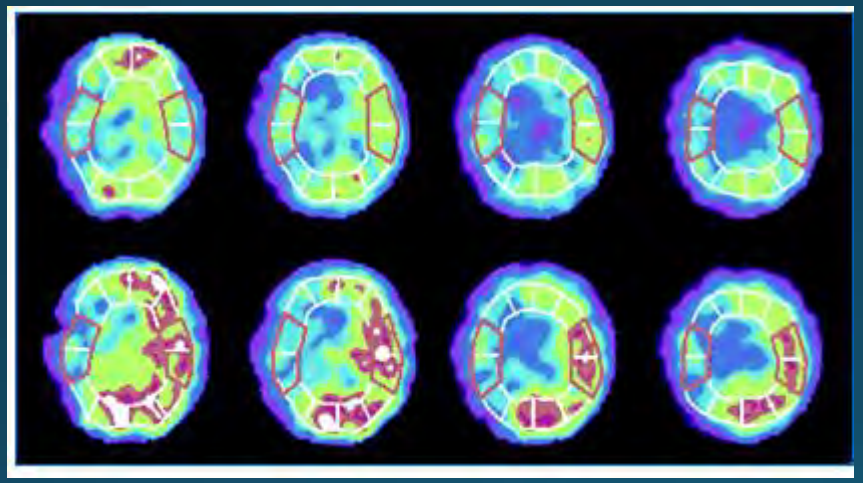
Xe CBF rest/Xe CBF after ACZ; CPR is defined as percentage increase in CBF after ACZ enhancement, or CPR = [(CBF [ACZ] - CBF [rest])/CBF (rest)] x 100 (%).



http://jnm.snmjournals.org/cgi/content/full/43/12/1616

a. Tc99m-HMPAO unstabilized
b. Tc99m-HMPAO stabilized
c. Tc99m-ECD

2. Radiopharmaceutical Preparation

- a. Use fresh generator eluate (<2 hr old) for optimal results with Tc99m-HMPAO.
- b. Do not use pertechnetate obtained from a generator which has not been eluted for 24 hr or more.

- 3. Radiopharmaceutical Injection
- a. Tc99m-HMPAO (unstabilized): Inject tracer no sooner than 10 min pre- and no more than 30 min post-reconstitution
- b. Tc99m-HMPAO (stabilized): Tracer should be injected no sooner than 10 min pre and no more than four hr post-reconstitution.
- c. Tc99m-Bicisate (ECD): Inject tracer no sooner than 10 min pre- and no more than 6 hr post-reconstitution.

Tc99m-HMPAO

- HMPAO is a lipophilic compound which is chemically unstable in-vitro (it undergoes oxidation).
- It has a first pass extraction of about 80%.
- The distribution of the tracer is proportional to the regional cerebral blood flow, however,

  the ratio of gray to white matter activity is about 2.5:1 compared to the 4:1 with Tc99m-ECD.
- Activity parallels cerebral blood flow up to 200 ml/min/100 gm of tissue (normal gray matter blood flow is about 80 ml/min/100 gm). HMPAO appears to overestimate low flow slightly, while underestimating areas of high flow.

- Due to rapid decomposition of the compound in vitro to a hydrophilic compound which will not cross the blood brain barrier, the agent must be used within 20-30 minutes of its preparation.
- A radiochemical purity of less than 85% or mixing the sample with blood in the syringe prior to injection results in poor image quality (the lipophilic agent will enter the RBC's).
- Stabilized forms of HMPAO using either methylene blue or cobalt chloride are available and allow easier labeling and improved image quality with reduced background activity
- luxury perfusion which can result in an inability to properly identify areas of nonviable brain

Normal distribution

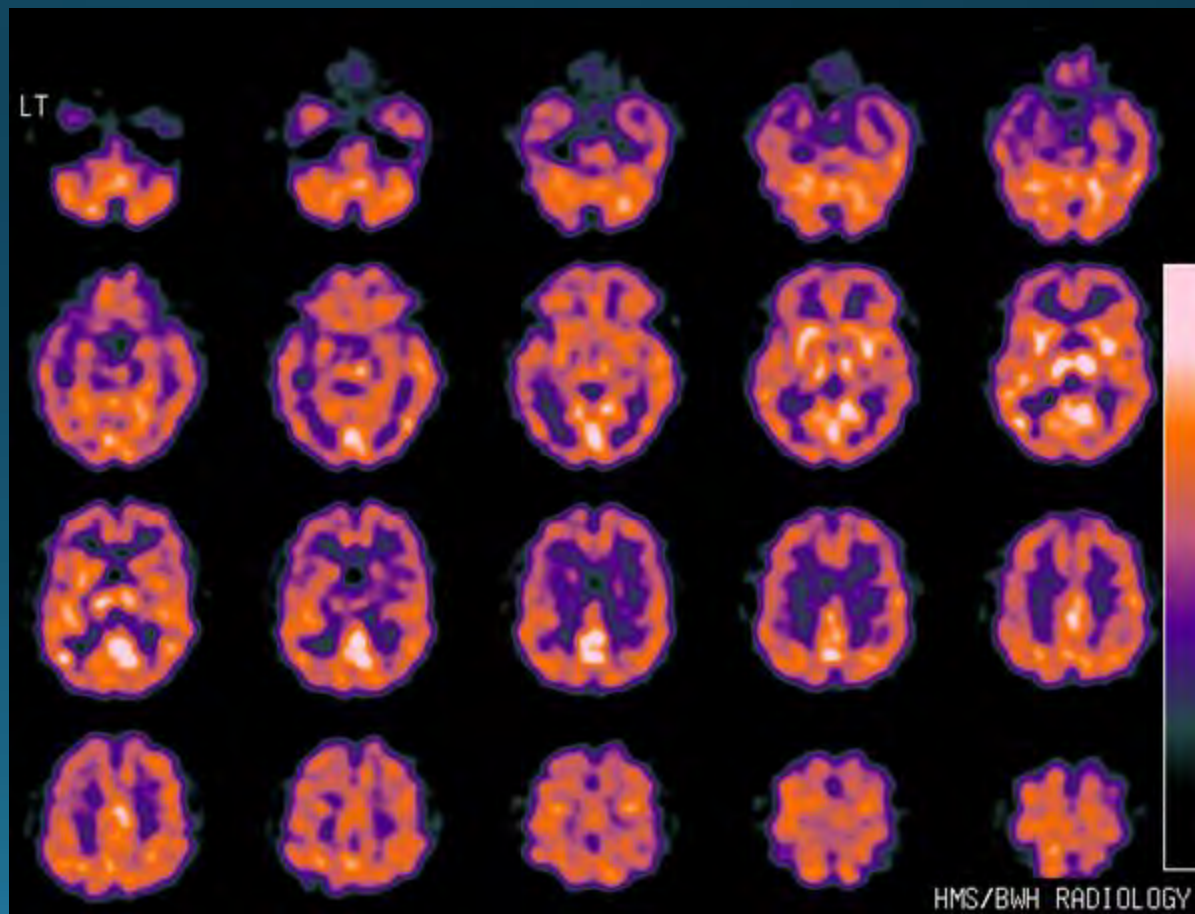
- Normally the frontal lobes, thalamus and cerebellum accumulates more radiotracer . Midline structures including the basal ganglia and thalami should be clearly evident and relatively symmetric. Eyes open

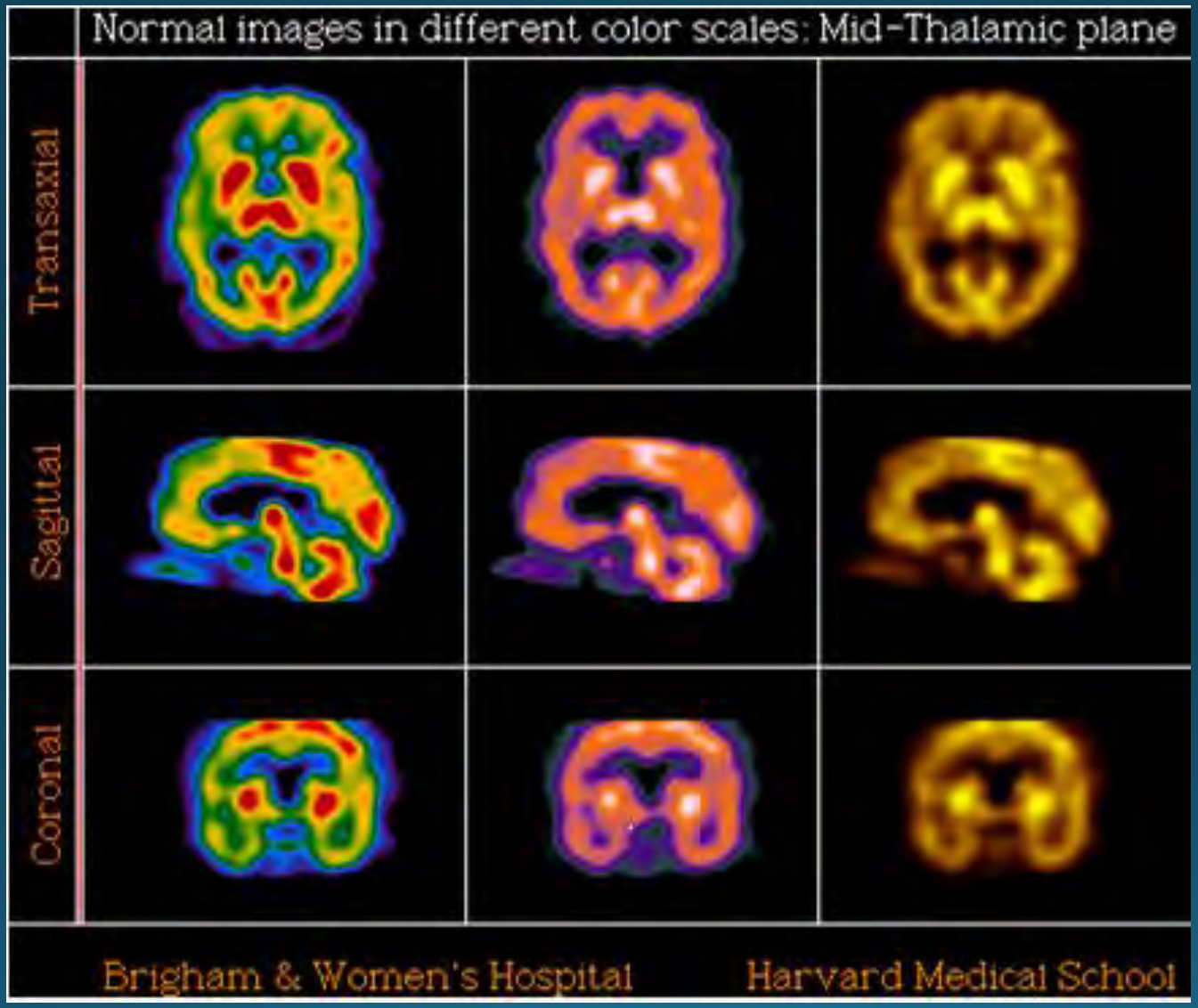
  or closed may increase

  or decrease, respectively,

  the visual cortex activity

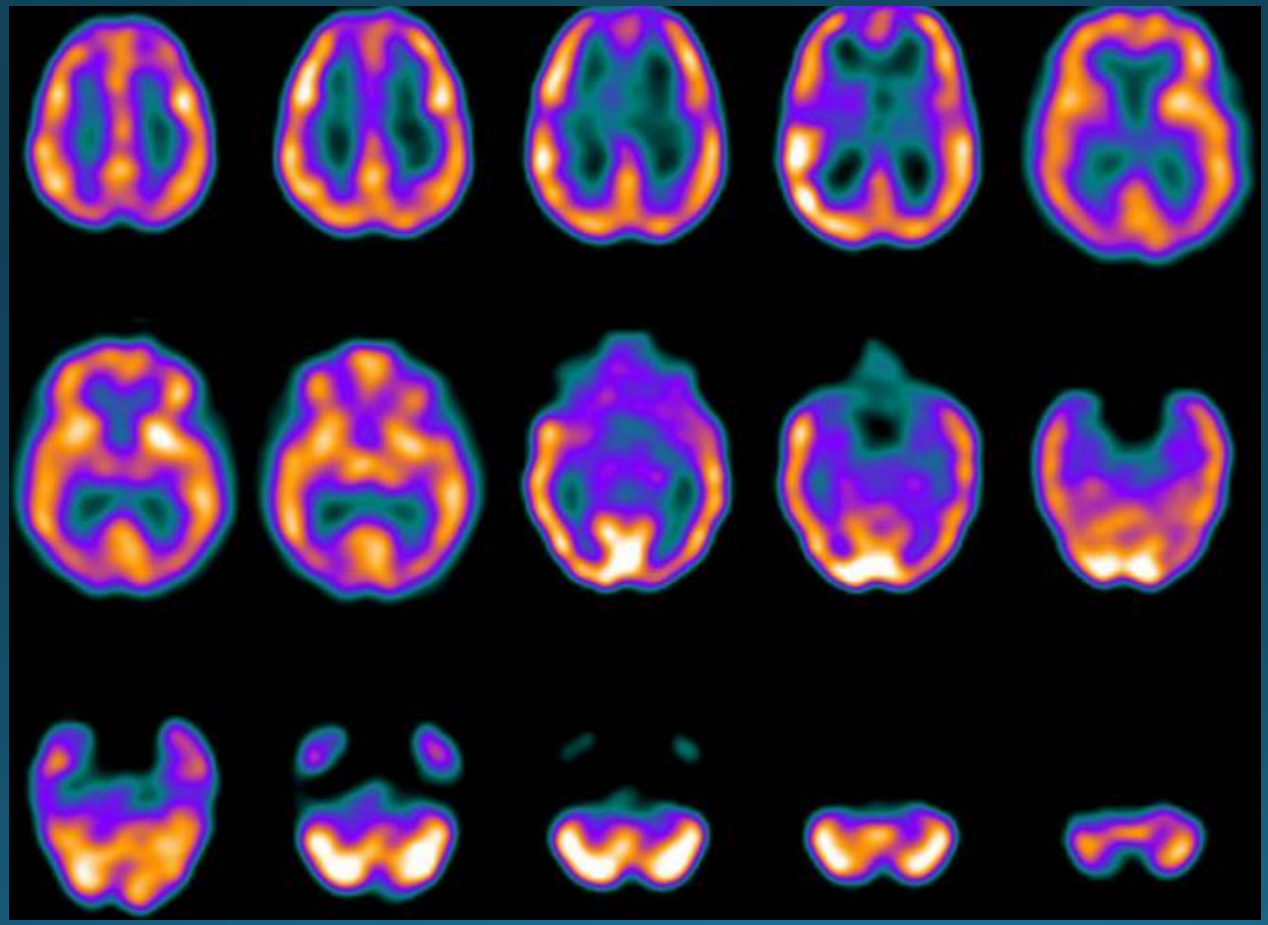
  by 30%




Normal images in different color scales: Mid-Thalamic plane
Transaxial
Sagittal
Coronal
Brigham & Women's Hospital
Harvard Medical School

Tc99m-ECD

- stable in-vitro (4 to 6 hours after reconstitution, as compared to less than 30 minutes for Tc99m-HMPAO)
- freshly eluted Tc-99m is not required for its preparation
- higher gray-to-white matter ratio
- In subacute infarcts, during the period of luxury perfusion, persistent defect due to altered esterase function in hypoxia (hypometabolism) which results in an inability to fix the agent intracellularly
- In other words, Tc-ECD is considered to be a perfusion marker of viable brain tissue



Radiation Dosimetry in Adults

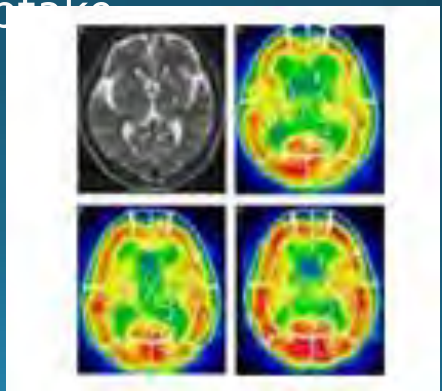
Radiopharmaceutical	Administered Activity MBq (mCi)	Organ Receiving the Largest Radiation Dose* mGy (rad)	Effective Dose* mSv (rem)
Tc-99m HMPAO[1]	555 – 1110 i.v. (15 – 30)	0.034 kidneys (0.126)	0.0093 (0.034)
Tc-99m ECD	555 – 1110 i.v. (15 – 30)	0.073 bladder wall (0.27)	0.011 (0.041)

Children

7.4–11.1 MBq/kg (0.2–0.3 mCi/kg). Minimum dose is 3–5 mCi.

I-123 IMP (d, I-N-isopropyl-p-iodoamphetamine hydrochloride):

- IMP has a high first pass extraction fraction of greater than 95% with a linear relationship between tissue activity and cerebral blood flow up to the high flow range
- Peak brain activity is reached within 20 minutes. The remainder of the tracer predominantly localizes to the lungs (33%), liver (45%), and kidney
- Imaging must be done promptly as IMP metabolites will washout and redistribute over time.
- In subacute strokes, during the period of luxury perfusion, in contrast to Tc99mHMPAO, IMP studies will still demonstrate a perfusion defect as the associated local acidosis decreases IMP up

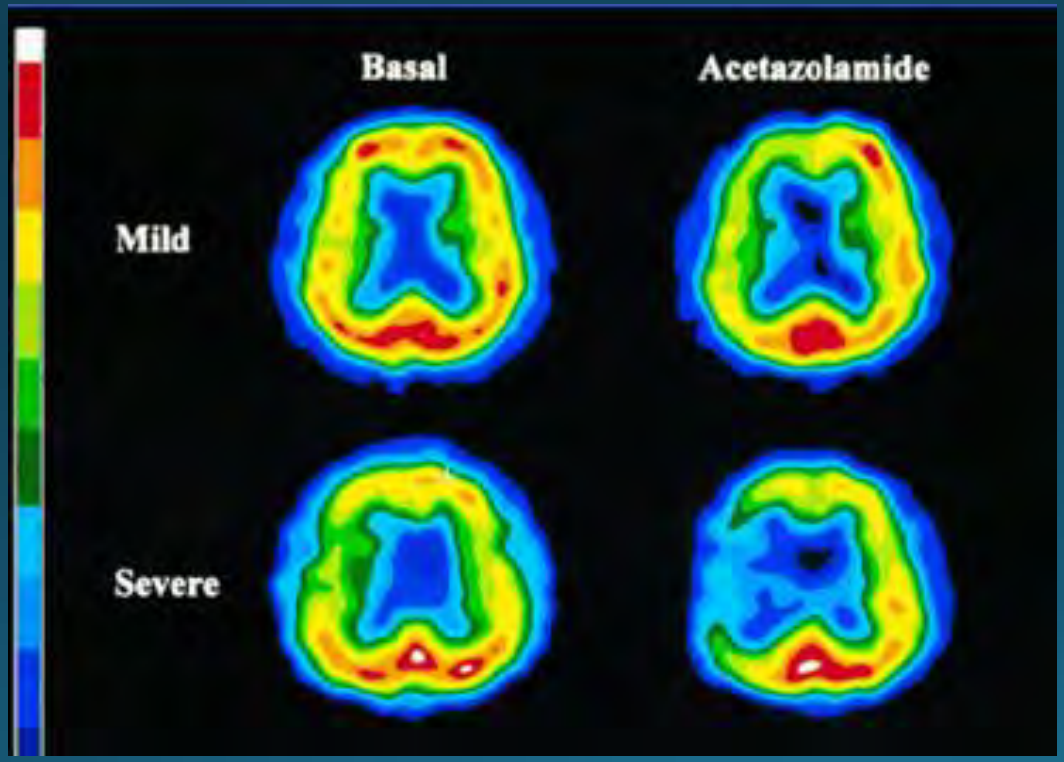


Indication of the test

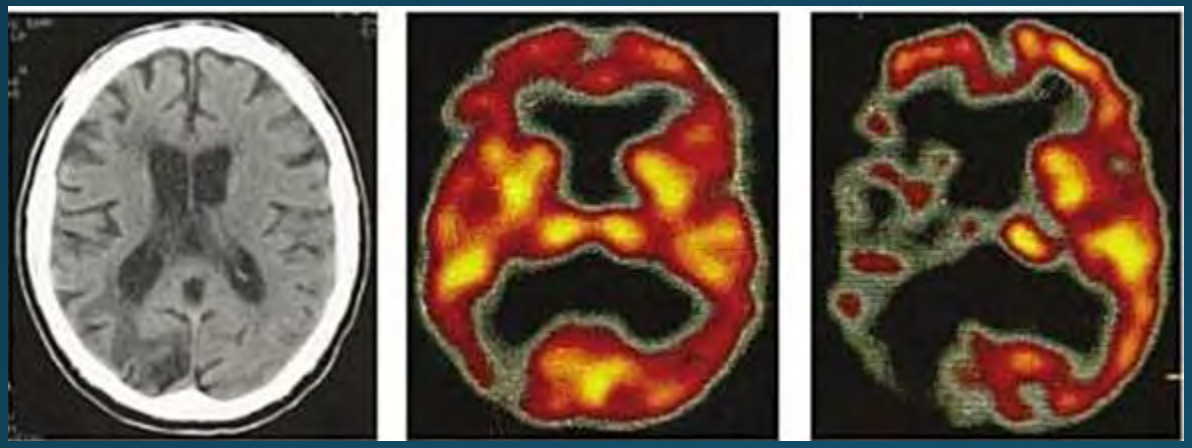
- Assessment of vascular reserve in patients with

1. Carotid stenosis
2. TIA
3. Cerebrovascular disease
4. Diabetes
5. Prior ECD-ICD by pass
6. Moya-Moya disease
7. Complementary method in determining selective carotid shunting during CEA

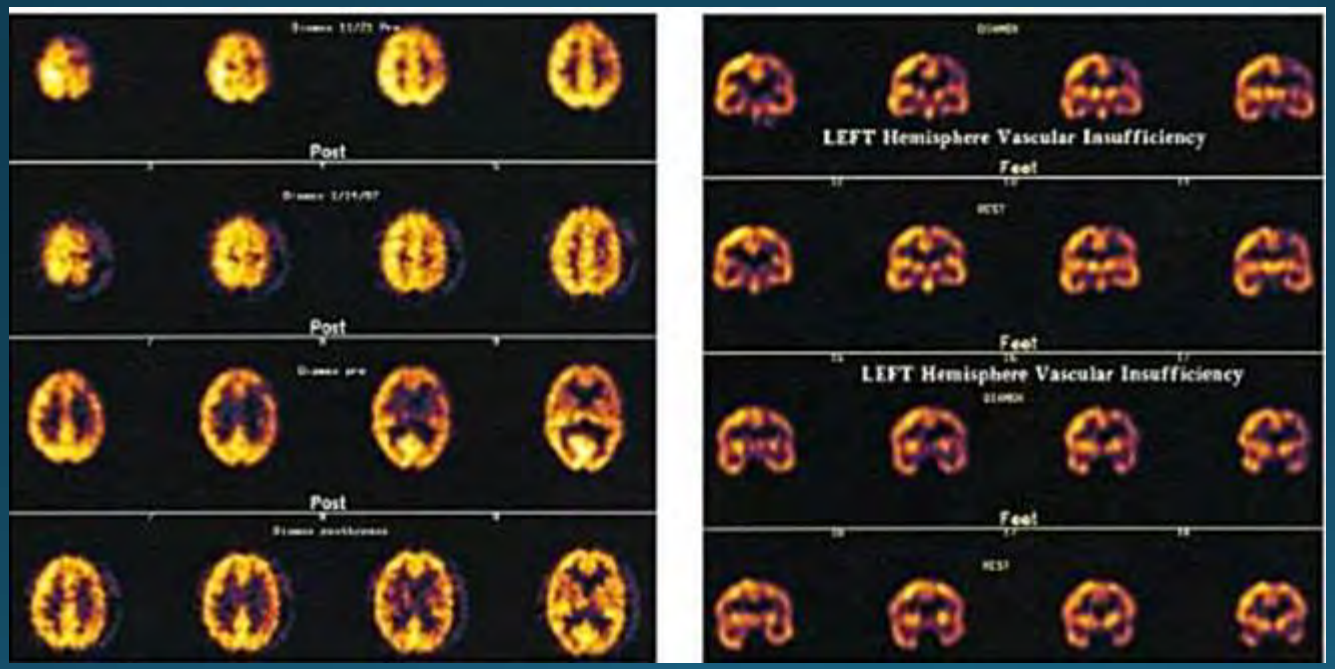
Complementary method in determining selective carotid shunting during carotid endarterectomy

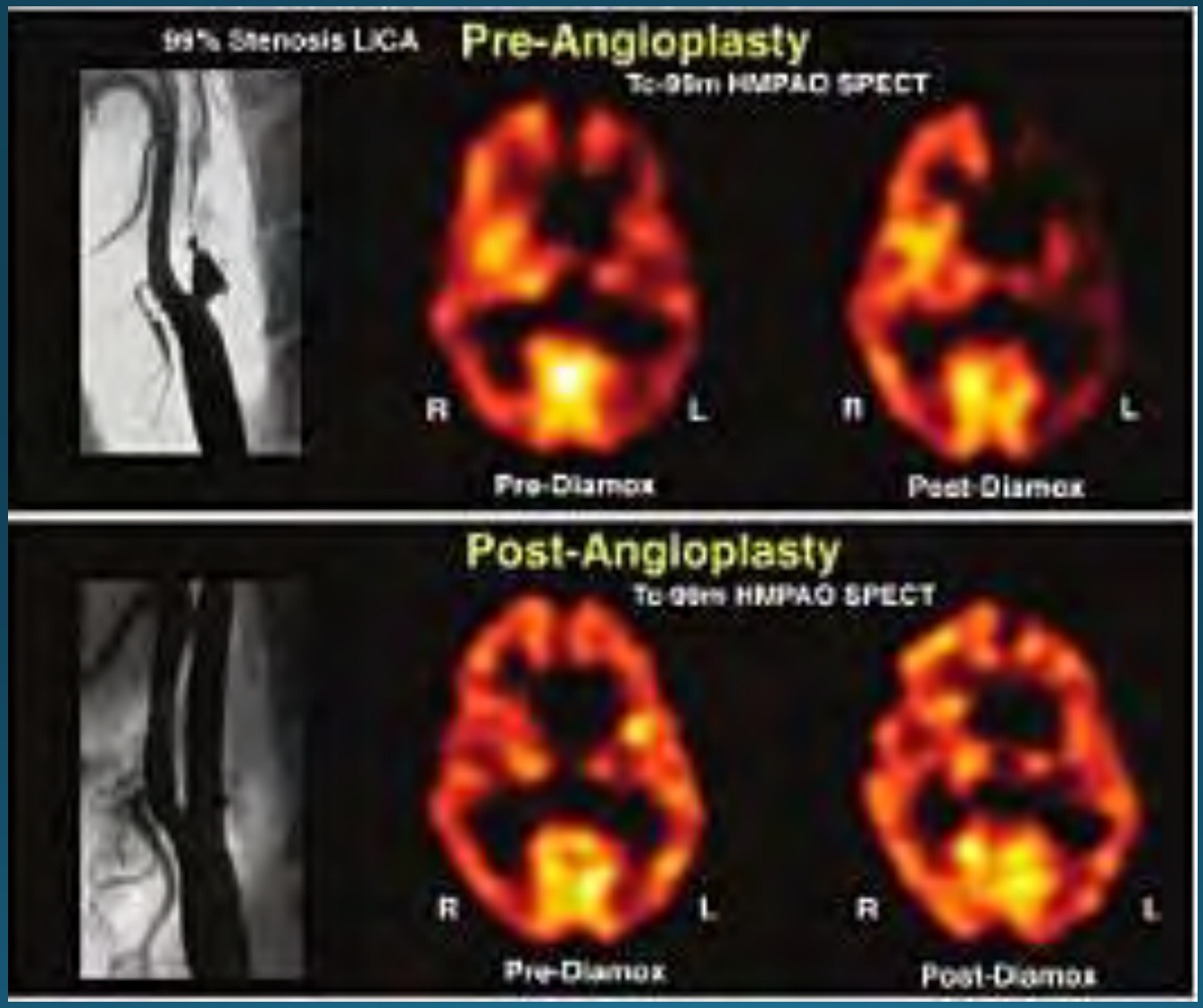


ACZ –Tc99m-HMPAO



Moya-Moya disease ACZ/postsurgery STA-MCA




99% Stenosis LICA
Pre-Angioplasty
Tc-99m HMPAO SPECT
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Pre-Diamox
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Post-Angioplasty
Tc 99m HMPAO SPECT
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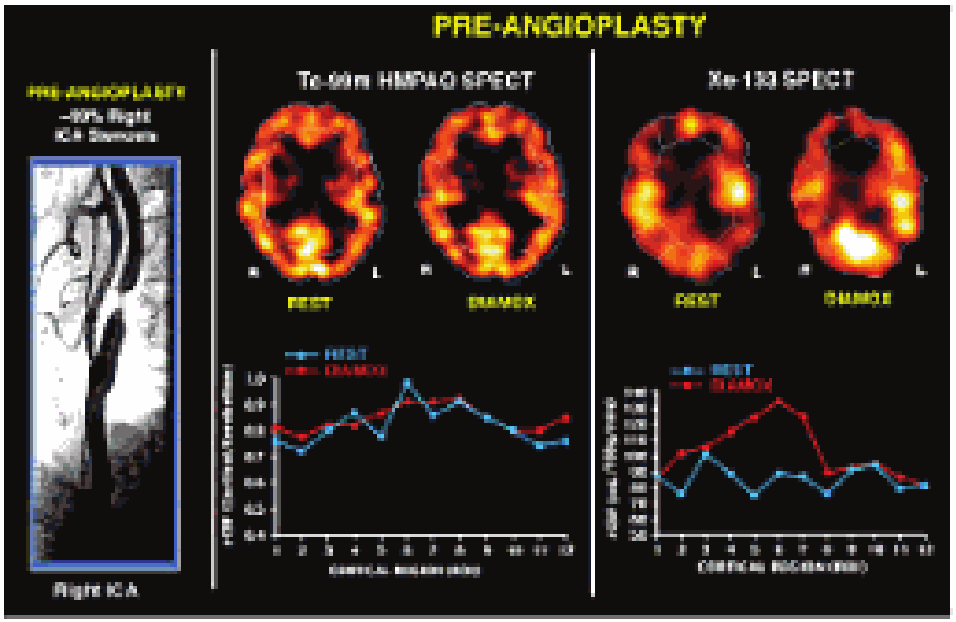
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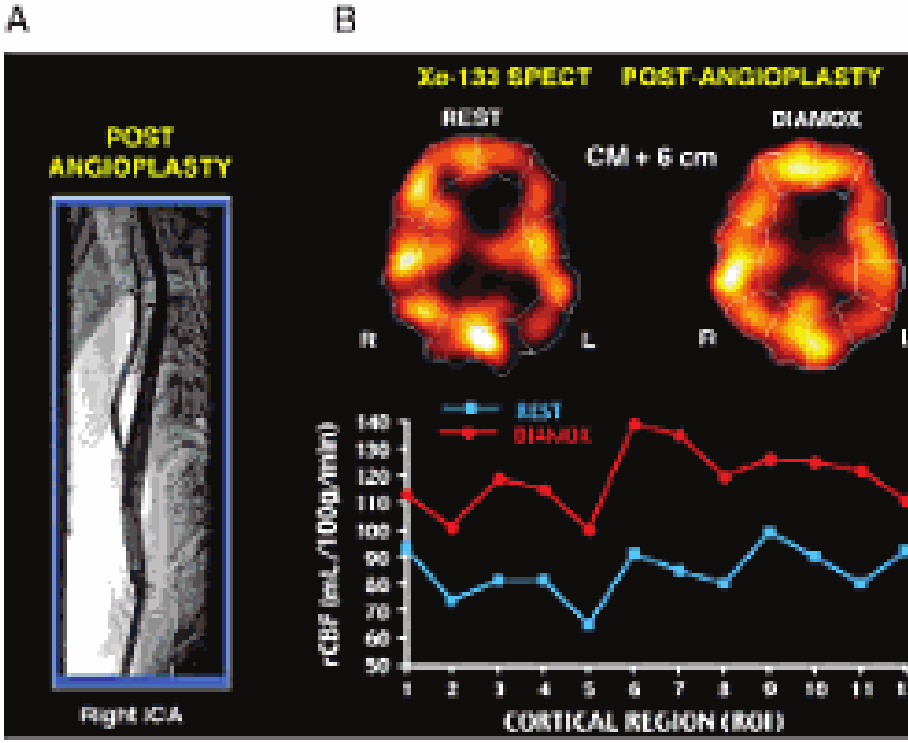
PRE-ANGIOPLASTY
Tc-99m HMPAO SPECT
Xe-133 SPECT
REST
DIAMOX
Right ICA


A
B
Xe-133 SPECT POST-ANGIOPLASTY
POST ANGIOPLASTY
REST
DIAMOX
CM + 6 cm
Right ICA
CORTICAL REGION (ROI)

Suggested Articles

1. Saremi F, et al. Radiographics 2002; Pharmacologic interventions in nuclear radiology: indications, imaging protocols, and clinical results. 22: 477-490.
2. Sugawara Y;J Nucl Med 2002;, et al. Usefulness of brain SPECT to evaluate brain tolerance and hemodynamic changes during temporary balloon occlusion test and after a permanent carotid occlusion. 43:1616-1623.
3. Sato Y,(18) J Nucl Med 2011; et al. Preoperative central benzodiazepine receptor binding potential and cerebral blood flow images on SPECT predict development of new cerebral ischemic events and cerebral hyperperfusion after carotid endarterectomy. 52: 1400-1407.
4. Sugawara Y,J Nucl Med 2001;, et al. Hyperactivity of 99mTc-HMPAO within 6 hours in patients with acute ischemic stroke. 42: 1297-1302