Cysteine Ethyl Ester Tc 99m

In the case of Neurolite®, the neutral lipophilic complex for imaging of brain blood perfusion passively crosses the blood-brain-barrier, and endogenous esterases convert one of the pendant ester groups to a charged carboxylate anion.

Cerebrovascular Ischemia

In Diagnostic Imaging: Nuclear Medicine (Second Edition), 2016

Nuclear Medicine Findings

- Tc-99m ECD/HMPAO SPECT with Diamox challenge: Assessment of functional cerebrovascular reserve in chronic stenotic occlusive diseaseoImages obtained with Diamox–Diamox is a carbonic anhydrase inhibitor that crosses the blood brain barrier and increases pCO2, which leads to increased blood flow in normal vessels–Vessels that are already maximally vasodilated due to stenosis will show decreased uptakeoDecreased activity in brain positive for inducible ischemia if same region normal baseline SPECToDiamox-only SPECT shows increased sensitivity over non-Diamox SPECT for detection of ischemic regions of clinical significance
- Wada test with Tc-99m ECD/HMPAO SPECT: Preoperative assessment prior to temporal lobectomy for epilepsyoInjection of sodium amobarbital to anesthetize a cerebral hemisphere to determine dominant hemisphere for speech/memory prior to surgeryoSimultaneous injection of Tc-99m ECD/HMPAO with subsequent SPECT imaging used to evaluate for collateral circulation resulting in amobarbital crossover to contralateral cerebral hemisphere
-

Balloon occlusion test (BOT) with Tc-99m ECD/HMPAO SPECT: Preoperative assessment prior to carotid sacrificeoCarotid sacrifice may be done for large en bloc surgical resection of skull base tumors or treatment of intracranial aneurysmsoBOT coupled with SPECT to assess regional blood flow prior to carotid artery sacrificeoBOT with SPECT typically requires 15-30 min occlusion time and transport of patient to multiple image suitesoIf decreased activity in region on BOT, consider baseline study to compareoTranscranial Doppler becoming imaging modality of choice secondary to decreased occlusion times and no need to move patient to separate image suiteoCerebral blood flow < 30 mL/100 g per min during total balloon occlusion at risk for ischemic stroke–Normal cerebral blood flow 54 mL/100 g per min (SD 12 mL/100 g per min)

- Tc-99m ECD/HMPAO SPECT: Postinterventional assessmentoSpasm or postinterventional vascular compromise: Decreased uptakeoPrediction of hyperperfusion syndrome following carotid and other bypass procedures: Increased uptake
- Tc-99m ECD/HMPAO SPECT: Cerebral infarction in problem or equivocal casesoAssessment of penumbra at risk for extension of infarction: Decreased perfusion surrounding region of infarctionoAssessment of subacute infarction: Small amounts of perfusion in regions of suspected infarction may support salvage procedure
- Additional nuclear medicine imaging optionsoXe-133 SPECT, XeCT, and O-15 H2O PET: Assessment of regional cerebral blood flow; primarily used in research–Gold standard methods for quantifying (PET) or comparing (SPECT, CT) regional cerebral flood flowoTc-99m diethylenetriaminepentaacetic acid (DTPA) SPECT: Assessment of blood brain barrier disruption (BBBD)–Magnitude of disruption (> 2.5x opposite normal side) correlates with lack of functional recovery

> Read full chapter

Gamma camera imaging in ischemic diseases of CNS

Madhavi Tripathi, in Reference Module in Biomedical Sciences, 2022

Tc-99m ECD

Tc-99m bicisate (Neurolite) is a neutral lipophilic agent that diffuses passively across the BBB like Tc-99m HMPAO. Once radiolabeling is complete, Tc-99m ECD is stable for upto 6 h and can be safely injected.

It has a first-pass extraction of 60–70%, with peak brain activity reaching 5–6% of the injected dose. The blood clearance of Tc-99m ECD is more rapid than Tc-99m HMPAO, at 1 h, less than 5% of the dose remains in the blood, compared with more than 12% of a Tc-99m HMPAO.

This results in better brain-to-background ratios for Tc-99m ECD (images are superior to those with Tc-99m HMPAO at 15–30 min after injection). Once inside the cell, Tc-99m ECD undergoes enzymatic de-esterification, forming polar metabolites which are unable to cross the cell membrane (Jacquier-Sarlin et al., 1996).

Almost 25% of the brain activity clears by 4 h with slow (roughly 6% per hour) washout of some of the labeled metabolites, thus images may be suboptimal if delayed. Ideally imaging is started after 45 min to allow for background clearance. The uptake pattern of these two tracers has been reported to show some differences in normal subjects and in stroke patients (Hyun et al., 2001; Shishido et al., 1995) (Table 1).

> Read full chapter

Brain

In Imaging in Neurology, 2016

Nuclear Medicine Findings

- PEToParietooccipital hypometabolism = most conspicuous finding in MR-negative NPSLE
- Tc-99m ethyl cysteinate dimer brain SPECToSensitive tool for early detection of brain abnormalities in SLE (more sensitive than MR)oRelatively nonspecific regional cerebral cortical hypoperfusion–Most hypoperfused areas: Parietal, frontal, and temporal lobes (MCA territory)–Least hypoperfused area: CerebellumoPositive findings also seen in patients without neuropsychiatric signs/symptoms–Secondary to subclinical brain involvement or cerebral atrophy (due to steroid therapy)–Occasionally may show transient hyperperfusion

> Read full chapter

Brain Death

In Diagnostic Imaging: Brain (Third Edition), 2016

IMAGING

General Features

- Best diagnostic clue○ No flow in intracranial arteries or venous sinuses on Tc-99m ECD (Neurolite)
- Imaging may confirm but does not substitute for clinical criteria

CT Findings

- NECT○ Diffuse cerebral edema (GM-WM borders effaced)□White cerebellum sign (sometimes called cerebellar "reversal" sign with density of cerebellum >> hemispheres)□Pseudosubarachnoid appearance due to venous congestion in effaced sulci○ Swollen gyri; compressed ventricles/cisterns
- CECT○ No enhancement of intracranial arteries, veins
- CTA○ Useful confirmatory or add-on test for BD○ Does not replace neurological testing○ No intravascular enhancement□Lack of opacification of MCA cortical branches and internal cerebral veins (ICVs) highly specific to confirm brain death

MR Findings

- T1WI○ Hypointense, swollen cortex ± gray-white matter differentiation loss○ Sulci, cisterns obliterated
- T2WI○ Cortex hyperintense, gyri swollen
- T2* GRE○ Cortical, medullary veins hypointense □Stagnant flow with deoxyhemoglobin
- DWI○ Hemispheric high signal, severe ADC drop□DWI improves sensitivity for predicting poor outcome by 38%; in combination with 72-hour neuro exam, it is 100% specific–Best between 49 and 108 hours after arrest○ Diffusion anisotropy diminishes 1-12 hours after BD
- T1WI C+○ No intracranial vascular enhancement
- MRA○ No intracranial flow
- MRS○ Pediatric reports show inorganic phosphate with phosphodiester and absence of ATP and phosphocreatine□Phosphocreatine detectable in healthy

brainsoNAA/Cho ratio (< 1.6) has been shown to help differentiate patients with poor outcomes

Ultrasonographic Findings

- Orbital DoppleroAbsence/reversal of end-diastolic flow in ophthalmic, central retinal arteriesoMarkedly increased arterial resistive indices
- Transcranial DoppleroGlobal circulatory arrestoOscillating "to and fro" signaloCaution: 20% have ICA flow demonstrated despite cerebral circulatory arrest

Angiographic Findings

- ConventionaloNo intracranial flowoContrast stasis (ECA fills, supraclinoid ICA does not)

Nuclear Medicine Findings

- Tc-99m-labeled exametazime scintigraphyoAbsent intracranial uptake ("light bulb" sign)oIncreased extracranial activity ("hot nose" sign)

Other Modality Findings

- EEG isoelectric

Imaging Recommendations

- Best imaging tooloEEG plus bedside scintigraphy (Neurolite)oEvoked potentials enables neurofunctional evaluation of comatose patient

> Read full chapter

CENTRAL NERVOUS SYSTEM

In Specialty Imaging: PET, 2018

Nuclear Medicine Findings

- SPECT perfusionoRadiotracer deposition reflects regional cerebral blood flow–Tc-99m hexamethylpropyleneamine oxime (HMPAO) and Tc-99m ethyl cysteinate dimer (ECD) most commonly used tracers□Lipophilic, small molecules diffuse across blood-brain barrier□ECD clears more rapidly from blood pool, has more linear extraction at high blood flow rates; less nonspecific scalp and

soft tissue uptake than HMPAO–High 1st-pass extraction, peak accumulation in ~ 2 min, no substantial redistribution□Can image for at least 2 h after injection without substantial loss of fidelity○Interictal SPECT–Epileptogenic focus appears as area of decreased radiotracer deposition (hypoperfusion)-○Ictal SPECT–Epileptogenic focus appears as area of increased radiotracer deposition (hyperperfusion)□Correspondence to epileptogenic focus depends on interval between seizure onset and injection; longer intervals allow more propagation to surrounding tissue□Beware of pseudonormalization where hyperperfusion during ictus makes baseline hypoperfused focus appear symmetric to normal side–Higher sensitivity than interictal SPECT for epileptogenic focus

> Read full chapter

Pearls, Pitfalls, and Frequently Asked Questions

In Nuclear Medicine (Fourth Edition), 2014

Central Nervous System

Q: How is the diagnosis of brain death made?

A: This is mainly a clinical diagnosis, typically made in a patient in deep coma with total absence of brainstem reflexes and spontaneous respiration. Reversible causes must be excluded (e.g., drugs, hypothermia), the cause of the dysfunction must be diagnosed (e.g., trauma, stroke), and the clinical findings of brain death must be present for a defined period of observation (6-24 hours). Confirmatory tests such as electroencephalography (EEG) and radionuclide brain flow imaging may be used to increase diagnostic certainty.

Q: Which radiopharmaceuticals are used to evaluate brain death and what are the advantages of each?

A: Tc-99m DTPA is inexpensive but more technically demanding to use and interpret. Tc-99m HMPAO or Tc-99m ethyl cysteinate dimer (ECD) are often preferred because no flow study is required, only delayed planar images to visualize radiotracer fixed in cerebral cortex.

A Pearl

A "hot nose" may be seen on the flow-phase images and delayed images as a result of shunting of blood from the internal to the external carotid system supplying the face and nose.

Q: What is the mechanism of uptake for the Tc-99m cerebral perfusion agents?

A: Tc-99m HMPAO and Tc-99m ECD are lipid-soluble cerebral perfusion agents taken up in proportion to regional cerebral blood flow. They fix intracellularly.

A Pearl

In most clinical situations, cerebral blood flow follows metabolism. An exception is the decoupling of metabolism and blood flow seen during the acute phase of a stroke. Blood flow may be normal or increased for the initial 1 to 10 days (luxury perfusion), but metabolism is decreased.

Q: How can SPECT brain perfusion or FDG PET imaging be useful in the differential diagnosis of dementia?

A: By noting the distribution pattern. Multiinfarct dementia is characterized by multiple areas of past infarcts, recognized as areas of decreased uptake that correspond to vascular distribution, and changes in the deep structures, such as the basal ganglia and thalamus. Alzheimer disease exhibits a characteristic pattern of bitemporal and parietal hypoperfusion and hypometabolism. Pick disease has decreased frontal lobe uptake.

A Pearl

Although Alzheimer disease has a characteristic bitemporal-parietal pattern on perfusion imaging*, it is often* not *symmetric and decreased frontal lobe uptake also may be seen in late-stage disease.*

Q: What is the purpose of cerebral perfusion imaging in patients with seizures? What is the expected PET or SPECT pattern?

A: Interictal studies are performed in patients unresponsive to medical therapy, requiring surgery for seizure control. Interictally, a seizure focus will show decreased metabolism on FDG PET and decreased perfusion on SPECT; increased activity is seen during a seizure (ictal). In some surgical seizure centers, depth electrodes are not required preoperatively if the clinical picture, EEG, and SPECT or PET study are all consistent as to the location of the seizure focus.

Q: Name the radiopharmaceutical used for cisternography and the most common clinical indication for this study.

A: In-111 DTPA is the most commonly used. The most common use of this radiopharmaceutical in modern practice is to localize shunt patency or cerebrospinal fluid leaks. Shunt patency studies can use In-111 DTPA or Tc-99m DTPA because of the short duration of the study.

> Read full chapter

Gamma camera imaging in movement disorders

Madhavi Tripathi, in Reference Module in Biomedical Sciences, 2022

Perfusion imaging

Resting brain perfusion studies in patients with movement disorders can be done using the lipophilic tracers Tc-99m hexamethylpropylamineoxime (HMPAO), Tc-99m Ethyl cysteinate dimer (ECD). 'Resting-state' measures of regional glucose utilization in the brain are evaluated using F-18 FDG PET. PD and the PS have characteristic metabolic patterns (Eidelberg et al., 1994; Antonini et al., 1998; Blin et al., 1990) that have been validated as metabolic signatures of the disease process. These metabolic phenotypes have been implemented for the differential diagnosis of idiopathic PD from the PS and also for differentiating amongst the PS using visual and quantitative approaches like statistical parametric mapping (SPM) (Eckert et al., 2005; Tripathi et al., 2013). Similar patterns have also been demonstrated on perfusion imaging using SPECT (Feigin et al., 2002) tracers (Table 3).

Table 3. Advantage and limitations of different imaging techniques in Parkinsonism-.

	SPECT Imaging-Dopaminergic	SPECT Imaging:Perfusion	Conventional radiological techniques	MRI
Advantages	In vivo demonstration of presynaptic dopaminergic dysfunction even in early disease.Differentiate DLB from AD.	Demonstrates specific perfusion patterns that can differentiate PS of PSP, MSA and CBS.	Evaluation of gross structural abnormality-Calcific densities in brain	No radiation involved.MRI is more often used to rule out other conditions like demyelination, vascular insults and normal pressure hydrocephalus besides others.The advanced cases may show hyperintense signal changes on T2 weighted images in bilateral substantia nigra as

				the only finding (Savoiardo, 2003).Few classical signs may be noted in Parkinson's plus syndromes of PSP (Oba et al., 2005) and MSA (Schrag et al., 2000).
Limitations	Cannot differentiate between Parkinsonian subtypes.Radiation exposure	Radiation exposure	No classical findings in Parkinson's disease.	Maybe unremarkable in early disease.

Characteristic patterns for perfusion are seen in PD and in the Parkinson-plus group- MSA, PSP, and DLB (Laere et al., 2004). PD is characterized by a pallido-thalamic, pontine and cerebellar hyper-perfusion, while MSA shows a putaminal hypoperfusion and PSP shows generalized hypoperfusion in the basal ganglia and anterior cingulate cortices. Disease related patterns on 'resting-state' can be applied to individual SPECT perfusion scans to provide group discrimination between PD patients, healthy controls, and MSA (Feigin et al., 2002; Laere et al., 2004; Bosman et al., 2003). A significant PD-related covariance pattern has been identified in perfusion SPECT data using network analysis. This pattern is characterized by relative increases in cerebellar, basal ganglia, and thalamic perfusion covarying with decrease in the frontal operculum and in the medial temporal cortex. This PD-related pattern expression discriminated PD from MSA patients. Fully automated voxel-based network assessment techniques using spatial covariance analysis can be used to quantify network expression in the ECD SPECT scans of parkinsonian patients (Eckert et al., 2007). Using age- and gender-matched healthy volunteer data and anatomical standardization, discriminant analysis has been used to differentiate between IPD and MSA (Bosman et al., 2003) with high discriminating power in clinically relevant circumstances.

> Read full chapter

Brain Death

In Diagnostic Imaging: Nuclear Medicine (Second Edition), 2016

Imaging Recommendations

•

Protocol adviceoPatient preparation–Confirm patient has stable blood pressure and is normally ventilated–Tourniquet encircling head can diminish scalp blood flowoRadiopharmaceutical–Brain parenchyma: Tc-99m HMPAO or Tc-99m ECD–Brain blood flow: Tc-99m DTPA or Tc-99m pertechnetate, but not recommendedoDose–Brain parenchyma: 15-20 mCi (555-740 MBq) for adults; 0.3 mCi/kg for children–Brain blood flow: Up to 30 mCi (1.1 GBq)-oDosimetry–Brain parenchyma agents: Kidneys and bladder receive highest radiation dose–Brain blood flow agents: Not recommended□Tc-99m DTPA: Bladder wall receives highest doseoImage acquisition–Gamma camera with field of view large enough to image entire head and neck–Portable gamma camera useful for bedside imaging in ventilated patient in intensive care unit–Flow images□Brain parenchyma: Image acquisition starting at time of radiotracer injection and ending well after venous phase□1-3 sec per frame for at least 60 sec□Brain angiogram: Tracer flow should be observed from level of carotids to skull vertex–Static planar images□Brain parenchyma: Anterior and lateral planar views should be obtained after at least 20 min□Brain angiogram: Anterior, posterior, and lateral view□Chin slightly tucked on lateral view to allow visualization of posterior fossa–SPECT□May be obtained in addition to flow and planar images with brain parenchyma tracers□Allows better visualization of perfusion to posterior fossa and brainstem structures□More difficult than bedside planar images with portable gamma cameraoReporting recommendations–Cerebral and cerebellar perfusion absent–Cerebral and cerebellar perfusion present–Cerebral and cerebellar perfusion present, although abnormal (discuss specific regions of uptake/lack of uptake)oIf equivocal, may repeat exam with 2x dose in 6 hrs or regular dose in 24 hrs

> Read full chapter

Neuroimaging of Dementia

J.C. Masdeu, in Encyclopedia of Human Behavior (Second Edition), 2012

Regional cerebral perfusion studied with SPECT

The most commonly used tracers for studying cerebral perfusion with SPECT are ^{99m}Tc HMPAO (hexamethyl propylamine oxime, Ceretec™), a lipid-soluble macrocyclic amine, and ^{99m}Tc ECD (ethyl cysteinate dimer, Neurolite™). The pattern of decreased regional perfusion in parietotemporal cortex, hippocampus, anterior and posterior cingulum, and dorsomedial and anterior nucleus of the thalamus had a sensitivity of 86% and a specificity of 80% for AD compared to normal controls. In a group of 70 patients with dementia and 14 controls, all with autopsy, SPECT

was most useful when the clinical diagnosis was of possible AD, with a probability of a diagnosis of AD of 67% without SPECT, of 84% with a positive SPECT, and of 52% with a negative SPECT. Although perfusion SPECT is less expensive and more readily available than FDG-PET, the consensus is that PET is slightly more sensitive and specific than SPECT for the diagnosis of mild AD, but it is clearly better for the differential diagnosis of vascular dementia.

> Read full chapter