

Society of Nuclear Medicine Procedure Guideline for Brain Perfusion Single Photon Emission Computed Tomography (SPECT) Using Tc-99m Radiopharmaceuticals

version 2.0, approved February 7, 1999

Authors: Jack E. Juni, MD (William Beaumont Hospital, Royal Oak, MI); Alan D. Waxman, MD (Cedars Sinai Medical Center, Los Angeles, CA); Michael D. Devous, Sr., PhD (University of Texas South West Medical Center, Dallas, TX); Ronald S. Tikofsky, PhD (College of Physicians and Surgeons of Columbia University, Harlem Hospital Affiliation, New York, NY); Masanori Ichise, MD (Mount Sinai Hospital and University of Toronto, Toronto, Ontario, Canada); Ronald L. Van Heertum, MD (Columbia-Presbyterian Medical Center, New York, NY); B. Leonard Holman, MD (Brigham and Women's Hospital, Boston, MA); Robert F. Carretta, MD (Sutter Roseville Medical Center, Roseville, CA); and Charles C. Chen, MD (Saint Francis Medical Center, Peoria, IL).

I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of brain perfusion SPECT studies using Tc-99m radiopharmaceuticals.

II. Background Information and Definitions

Single Photon Emission Computed Tomography (SPECT) of the brain is a technique for obtaining tomographic images of the 3-dimensional distribution of a radiopharmaceutical, which reflects regional cerebral perfusion.

III. Common Indications

- A. Detection and evaluation of cerebrovascular disease
- B. Evaluation of patients with suspected dementia
- C. Presurgical localization of epileptic foci
- D. Evaluation of suspected brain trauma

Additional indications not listed here are under active evaluation, many of which appear promising at this time.

IV. Procedure

A. Patient Preparation

1. Pre-Arrival

Patients should be instructed, if possible, to avoid caffeine, alcohol or other drugs known to affect cerebral blood flow (CBF).

2. Pre-Injection

- a. The most important aspect of patient preparation is to evaluate the patient for his/her ability to cooperate.
- b. Achieve a consistent environment at the time of injection and uptake:
 - i. Place the patient in a quiet, dimly-lit room.
 - ii. Instruct the patient to keep his/her eyes and ears open.
 - iii. Ensure that the patient is seated or reclining comfortably.
 - iv. Place intravenous access at least 10 min prior to injection to permit accommodation.
 - v. Instruct the patient not to speak or read.
 - vi. Have no interaction with the patient prior to, during or up to 5 min post-injection.

B. Information Pertinent to Performing the Procedure

Relevant patient data suggested for optimal interpretation of scans includes: patient history (including any past drug use or trauma), neurologic exam, psychiatric exam, mental status exam (e.g. Folstein mini-mental exam or other neuropsychological test), recent morphologic imaging studies (e.g. CT, MRI), current medication and when last taken.

C. Precautions

- 1. Demented patients must be closely monitored at all times.
- 2. Patients with neurologic deficits may require special care and monitoring.
- 3. If sedation is required, it should be given af-

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)

*per MBq (per mCi)

¹ICRP 62, page 13

ter injection of radiopharmaceutical, when possible.

D. Radiopharmaceutical

1. Radiopharmaceuticals

- Tc99m-HMPAO (Exametazime [unstable])
- Tc99m-HMPAO (Exametazime [stable])
- Tc99m-Bicisate (Ethyl cystine dimer [ECD])

2. Radiopharmaceutical Preparation

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

3. Radiopharmaceutical Injection

- Tc99m-HMPAO (unstable): Inject

tracer no sooner than 10 min pre- and no more than 30 min post-reconstitution. For seizure disorders, it is important to inject the tracer as soon as possible after reconstitution (within 1 min).

- Tc99m-HMPAO (stable): Tracer should be injected no sooner than 10 min pre- and no more than four hr post-reconstitution.

- Tc99m-Bicisate (ECD): Inject tracer no sooner than 10 min pre- and no more than 6 hr post-reconstitution.

- Patients should be instructed to void within 2 hr post-injection to minimize radiation exposure.

4. Delay Time from Injection to Imaging

- Tc99m-HMPAO (unstable and stable): ≥90 min delay from injection to

Radiation Dosimetry in Children (5 years old)

Radiopharmaceutical	Administered Activity MBq/kg (mCi/kg)	Organ Receiving the Largest Radiation Dose* mGy (rad)	Effective Dose* mSv (rem)
Tc-99m HMPAO ¹	7.4 – 11.1 i.v. (0.2 – 0.3)	0.14 thyroid (0.52)	0.026 (0.096)
Tc-99m ECD ²	7.4 – 11.1 i.v. (0.2 – 0.3)	0.083 bladder wall (0.31)	0.023 (0.085)

*per MBq (per mCi)

¹ICRP 62, page 13²Treves ST. *Pediatric Nuclear Medicine*, 2nd edition. Springer-Verlag, 1995, p. 576.

- imaging for best image quality. Images obtained after a 40 min delay will be interpretable.
- b. Tc99m-ECD: Approximately 45 min delay from injection to imaging for best image quality. Images obtained after a 20 min delay will be interpretable.
 - c. Imaging should be completed within 4 hr post injection if possible. Excessive delay should be avoided.
5. Dosage: Adults 555–1110 MBq (15–30 mCi Tc99m-HMPAO or Bicisate [ECD], typically 20 mCi [740 MBq] for HMPAO or 30 mCi [1110 MBq] for ECD). Children 7.4–11.1 MBq/kg (0.2–0.3 mCi/kg). Minimum dose is 3–5 mCi.
 6. Quality Control: Radiochemical purity determinations should be performed on each vial prior to injection using the method outlined in the package insert. A shortened one-step technique may also be used for Tc99m-HMPAO.
- E. Image Acquisition
- Set-up & acquisition
1. Multiple detector or other dedicated SPECT cameras generally produce results superior to single-detector general-purpose units. However, with meticulous attention to procedure, high-quality images can be produced on single-detector units with appropriately longer scan times (5 x 10⁶ total counts or more are desirable).
 2. Patient should void prior to study for maximum comfort during the study.
 3. The patient should be positioned for maximum comfort. Minor obliquities of head orientation can be corrected in most systems during processing.
 4. The patient's head should be lightly restrained to facilitate patient cooperation in minimizing motion during acquisition. It is not possible to rigidly bind the head in place. Patient cooperation is necessary. Sedation may be used following the injection of radiopharmaceutical if patient is uncooperative.
 5. Use the smallest radius of rotation possible with appropriate patient safeguards.
 6. Use of high-resolution or ultra high-resolution collimation is recommended. All purpose collimation is not suitable. As a general rule of thumb, use the highest resolution collimation available.
 7. Fan-beam or other focused collimators are generally preferable to parallel-hole as they provide improved resolution and higher count rates. Parallel-hole collimation is acceptable if adequate counts are obtained. Slant hole collimation may be used.
 8. A 128 x 128 or greater acquisition matrix should be used.
 9. Use 3° or better angular sampling. Acquisition pixel size should be 1/3–1/2 the expected reconstructed resolution. It may be necessary to use a hardware zoom to achieve an appropriate pixel size. Different zoom factors may be used in the x and y dimensions of a fan-beam collimator.
 10. Continuous acquisition may provide shorter total scan duration and reduced mechanical wear to the system when compared to step and shoot technique.
 11. Segmentation of data acquisition into multiple sequential acquisitions will permit exclusion of bad data, e.g. removing segments of projection data with patient motion.
 12. It is frequently useful to use detector pan and zoom capabilities to ensure that the entire brain is included in the field of view while allowing the detector to clear the patient's shoulders.
- F. Interventions
- Vasodilatory challenge with acetazolamide (Diamox) or equivalent.
- Indication: Evaluation of cerebrovascular reserve in TIA, completed stroke and/or vascular anomalies (e.g. arterial-venous malformation) and to aid in distinguishing vascular from neuronal causes of dementia.
- Acetazolamide (Diamox):
- Contraindications: Known sulfa allergy (skin rash, bronchospasm, anaphylactoid reaction). May induce migraine in patients with migraine history. Generally avoided within three days of an acute stroke.
- Various protocols have been used, including split-dose, two-day repeat study and dual-isotope techniques. The two-day repeat study technique is simplest and may therefore be preferable. Typically, the challenge portion is performed first. If this is normal, consideration may be given to omitting the baseline study. If a baseline scan is performed, allow sufficient time for residual activity to clear (typically 24 hr).
- Acetazolamide (Diamox):
- Dosage: Adults 1000 mg by slow iv push for typical patient. Children 14 mg/kg. Wait 15–20 min after administering acetazolamide before injecting tracer.
- Acetazolamide is a diuretic. The patient should be instructed to void immediately before beginning of image acquisition. Acquisition and

processing are identical to non-acetazolamide study.

Adverse effects: Mild vertigo, tinnitus, paresthesias and, rarely, nausea may be experienced. These are generally self-limited and do not require specific treatment. Patients may experience postural hypotension when arising and should be appropriately warned and assisted, if necessary.

G. Processing

Image Processing

1. Filter all studies in 3 dimensions (x, y and z). This can be achieved either by two-dimensionally prefiltering the projection data or by applying a 3-dimensional post-filter to the reconstructed data.
2. Low-pass (e.g., Butterworth) filters should generally be used. Resolution recovery or spatially varying filters should be used with caution, as they may produce artifacts.
3. When possible reconstruct the *entire* brain. Use care not to exclude the cerebellum or vertex.
4. Reconstruct data at highest pixel resolution, i.e. one pixel thick. If slices are to be summed, this should be done only after reconstruction and oblique reorientation (if performed).
5. Attenuation correction should be performed in all cases unless a specific application or circumstance would dictate otherwise. Use shape contouring if available. Be sure that contour includes scalp and not just gray matter. Whenever possible, the surface contour should be defined individually for each transaxial slice.
6. Reformat transaxial data into at least three orthogonal planes. Generate transverse sections relative to a repeatable anatomic orientation (e.g., AC-PC line), and coronal and sagittal sections orthogonal to the transverse. Additional sections along a plane parallel to the long axis of the temporal lobes are frequently useful.

H. Interpretation Criteria

1. The extent of normal variability must be appreciated during scan interpretation. Substantial variability may be noted between normal individuals and between scans of a single subject obtained at different times. Individual laboratories should obtain or be familiar with a normal database to best interpret patient studies. The Brain Imaging Council of the SNM is developing a publicly available database.
2. Unprocessed projection images should be reviewed in cinematic display prior to viewing

of tomographic sections. Projection data should be assessed for the presence and degree of patient motion, target-to-background ratio and other potential artifacts. Inspection of the projection data in sinogram form may also be useful.

3. Images should be viewed on a computer screen rather than from film or paper copy to permit interactive adjustment of contrast, background subtraction and color table.
4. Caution must be used in selecting levels of contrast and background subtraction. Non-continuous color scales may be confusing or misleading if abrupt color changes occur in the range of expected gray matter activity. Thresholding, if used, must be based upon knowledge of a normal database for specific radiopharmaceuticals and instruments used in acquiring the study. Artifacts can be created when inappropriate thresholding is performed.
5. Three-dimensional renderings may be useful in appreciating overall patterns of disease. Care must be exercised in choice of threshold, as artifactual defects are easily generated.
6. Images must be evaluated in the context of relevant structural information (CT/MRI). Specific attention should be paid to the extent of perfusion abnormalities relative to underlying morphologic defects (e.g. ischemic penumbra versus infarct) as well as to the possible effects of atrophy and partial-volume effect.
7. Epilepsy evaluation: Images must be correlated with the relevant EEG data and clinical observations in seizure patients. The exact timing of tracer injection relative to observed behavioral or electrical seizure activity must be known. The scintigraphic appearance and extent of seizure foci may change dramatically depending on the exact timing of tracer injection relative to seizure onset. Ictal and interictal studies should be compared for optimal patient evaluation. Ictal studies are more reliable for seizure foci localization.
8. Interpreters should be familiar with the document issued by the Ethical Subcommittee for Functional Brain Imaging, a subcommittee of the SNM Brain Imaging Council (see reference G, Mayberg, HS. The ethical clinical practice of functional brain imaging. *J Nucl Med* 1996;37:1256-1259).

I. Reporting

Study reports should describe the extent and severity of defects, their correlation with morphologic and clinical abnormalities and, when relevant, a differential diagnosis and/or the significance of abnormality. It must be recognized that many patients will present with non-specific perfusion patterns which cannot be directly attributed to a specific disorder or causative agent. Care must be taken to avoid implying the existence of cause and effect relationships between scan and behavioral/neurologic abnormalities.

Each clinical report should include the following:

1. Indications for the study (brief synopsis)
2. Assessment of the technical quality of the scan (good, adequate, poor, including presence of patient movement, deviations from usual lab protocol, etc., if relevant)
3. Description of abnormalities (including criteria for definition of abnormal, i.e. visual inspection criteria, regions of interest, comparison to lab database, reference paper, etc.)
4. Interpretation and conclusions
 - a. Provide a full differential diagnosis based on peer-reviewed and generally accepted disease-specific patterns. Any interpretive statements not based on such criteria should be explicitly identified as such.
 - b. As appropriate, qualify the scan interpretation in the context of known clinical history, associated co-morbid conditions, medications, and other diagnostic studies (CT, MRI, EEG). Alternatively, state the limitations of the offered differential diagnosis if relevant clinical data are not available, and recommend additional tests as indicated.
 - c. If the instrument and/or methodology used is significantly different than that which is typically used (e.g., as described in this guideline), the differences should be explicitly stated in the report. Any limitations of the study should be explicitly described.
 - d. If a study cannot be interpreted based on well-accepted criteria, the clinical report may, where relevant, include one or more statements similar to the following:
 - i. Although abnormalities are present in this study, there are no established cause and effect relationships between these observed abnormalities and the patient's clinical history or behavior in question.
 - ii. The abnormal pattern of increased or decreased activity in the [anatomical

area] is a pattern not proven by well-accepted, peer-reviewed published studies to be related to a specific disease entity.

- iii. The accumulation or reduction of activity in the [anatomical area] could be interpreted as an artifact associated with insufficient resolution or statistical variations.

J. Quality Control

See *Society of Nuclear Medicine Procedure Guideline for General Imaging*.

K. Sources of Error

1. Presence of sedating medications at the time of tracer injection may alter tracer distribution. If sedation is absolutely necessary it should, whenever possible, be administered at least 5 min after tracer injection. When sedation is used, record type and dosage of the sedative, and time at which sedative was administered in relation to time of tracer injection.
2. Patient motion during data acquisition may produce blurring of image data and may result in artifacts.

V. Issues Requiring Further Clarification

- A. Normal database issues
- B. Quantification techniques
- C. Coregistration techniques with MRI and CT

VI. Concise Bibliography

- Devous MD Sr. SPECT functional brain imaging. In: Kramer EL, Sanger J, eds. *Clinical SPECT Imaging*. Raven Press, Ltd., New York, NY 1995;97-128.
- Fayad PB, Brass LM. Single-photon emission computed tomography in cerebrovascular disease. *Stroke* 1991;22:950-954.
- Holman BL, Devous MD Sr. Functional brain SPECT: the emergence of a powerful clinical method. *J Nucl Med* 1992;33:1888-1904.
- Holman BL, Johnson KA, Garada B, et al. The scintigraphic appearance of Alzheimer's disease: a prospective study using technetium-99m-HMPAO SPECT. *J Nucl Med* 1992;33:181-185.
- Hung JC, Corlija M, Volkert WA, et al. Kinetic analysis of technetium-99m d, 1-HMPAO decomposition in aqueous media. *J Nucl Med* 1988;29:1568-1576.
- Juni JE. Taking brain SPECT seriously: reflections on recent clinical report in the Journal of Nuclear Medicine. *J Nucl Med* 1994;35:1891-1895.
- Mayberg, HS. The ethical clinical practice of functional brain imaging. *J Nucl Med* 1996;37: 1256-1259.
- Report of the Therapeutics and Technology Assess-

ment Subcommittee of the American Academy of Neurology. Assessment of brain SPECT. *Neurology* 1996;46:278-285.

Van Heertum RL, Miller SH, Mosesson RE. SPECT brain imaging in neurologic disease. *Radiol Clin North Am* 1993;31:881-907.

Van Heertum RL, Tikofsky RS (ed). *Cerebral Brain SPECT Imaging*. Raven Press, 2nd ed. New York City, NY: 1995.

VII. Disclaimer

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high-quality nuclear medicine procedures. These generic recommendations cannot be applied

to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different from the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend, in part, on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.