Procedure Guideline for Brain Perfusion SPECT Using ^{99m}Tc Radiopharmaceuticals 3.0*

Jack E. Juni[1], Alan D. Waxman[2], Michael D. Devous, Sr.[3], Ronald S. Tikofsky[4], Masanori Ichise[5], Ronald L. Van Heertum[6], Robert F. Carretta[7], and Charles C. Chen[8]

[1]William Beaumont Hospital, Royal Oak, Michigan; [2]Cedars Sinai Medical Center, Los Angeles California; [3]University of Texas Southwestern Medical Center, Dallas Texas; [4]College of Physicians and Surgeons of Columbia University, Harlem Hospital Affiliation, New York, New York; [5]Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada; [6]Columbia-Presbyterian Medical Center, New York, New York; [7]Sutter Roseville Medical Center, Roseville, California; and [8]Saint Francis Medical Center, Peoria, Illinois

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 ^{99m}Tc radiopharmaceuticals.

II. BACKGROUND INFORMATION AND DEFINITIONS

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. PROCEDURE

A. Patient Preparation

1. Before arrival, patients should be instructed to avoid, if possible, caffeine, alcohol, or other drugs known to affect cerebral blood flow.
2. Before injection:
   a. The most important aspect of patient preparation is to evaluate the patient for ability to cooperate.
   b. A consistent environment must be maintained at the time of injection and uptake:
      i. Place the patient in a quiet, dimly lit room.
      ii. Instruct the patient to keep eyes and ears open.
      iii. Ensure that the patient is seated or reclining comfortably.
      iv. Place intravenous access at least 10 min before injection to permit accommodation.
      v. Instruct the patient not to speak or read.
      vi. Have no interaction with the patient before, during, or for 5 min after 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 examination, psychiatric examination, mental status examination (e.g., Folstein mini-mental examination or other neuropsychologic tests), recent morphologic imaging studies (e.g., CT, MRI), and current medications 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 after injection of the radiopharmaceutical, when possible.

D. Radiopharmaceutical

1. Radiopharmaceutical types:
   a. Unstabilized ^{99m}Tc-exametazime (HMPAO)
   b. Stabilized ^{99m}Tc-HMPAO
   c. ^{99m}Tc-bicisate (ethyl cystine dimer [ECD])

Dosimetry for these radiopharmaceuticals is presented in Tables 1 and 2.

2. Radiopharmaceutical preparation:
   a. Use fresh generator eluate (<2 h old) for optimal results with ^{99m}Tc-HMPAO.
   b. Do not use pertechnetate obtained from a generator that has not been eluted for 24 h or more.
3. Radiopharmaceutical injection:
   a. Unstabilized ^{99m}Tc-HMPAO: Inject tracer no sooner than 10 min before and no more than 30 min after reconstitution. For seizure disorders, it is important to inject the tracer as soon as possible after reconstitution (within 1 min).
   b. Stabilized ^{99m}Tc-HMPAO: Inject tracer no sooner than 10 min before and no more than 4 h after reconstitution.

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For correspondence or reprints contact: Jack E. Juni, Academic Imaging Institute, 25595 York St., Royal Oak, MI 48067.
E-mail: jjuni@comcast.net
*YOU CAN ACCESS THIS ACTIVITY THROUGH THE SNM WEB SITE (http://www.snm.org/guidelines).

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TABLE 1
Radiation Dosimetry in Healthy Adults

Radiopharmaceutical	Administered activity (intravenous)		Organ receiving largest radiation dose		Effective dose	
	MBq	mCi	mGy	rad/mCi	mSv	rem/mCi
^{99m}Tc-HMPAO*	555–1,110	15–30	0.034 (kidneys)	0.126	0.0093	0.034
^{99m}Tc-ECD	555–1,110	15–30	0.073 (bladder wall)	0.126	0.011	0.041

*Data are from ICRP 62, page 13.

c. ^{99m}Tc-ECD: Inject tracer no sooner than 10 min before and no more than 6 h after reconstitution.
d. Instruct patients to void within 2 h after injection to minimize radiation exposure.

4. Time delay from injection to imaging:
   a. ^{99m}Tc-HMPAO (unstabilized and stabilized): A 90-min delay from injection to imaging gives the best image quality. Images obtained after a 40-min delay will be interpretable.
   b. ^{99m}Tc-ECD: Approximately a 45-min delay from injection to imaging gives the best image quality. Images obtained after a 20-min delay will be interpretable.
   c. Imaging should be completed within 4 h after injection, if possible. An excessive delay should be avoided.
5. Dosage: Adults, 555–1,110 MBq (15–30 mCi) for ^{99m}Tc-HMPAO or ^{99m}Tc-ECD (typically 740 MBq [20 mCi] for ^{99m}Tc-HMPAO or 1,110 MBq [30 mCi] for ^{99m}Tc-ECD); children, 7.4–11.1 MBq/kg (0.2–0.3 mCi/kg). Minimum dose is 111–185 MBq (3–5 mCi).
6. Quality control: Radiochemical purity should be determined on each vial before injection using the method outlined in the package insert. A shortened 1-step technique may also be used for ^{99m}Tc-HMPAO.

E. Image 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 (5×10^6 total counts or more are desirable).
2. The patient should void before the 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 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 after injection of the radiopharmaceutical if the 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. Fanbeam or other focused collimators are generally preferable to parallel-hole, as they provide improved resolution and higher counting rates. Parallel-hole collimation is acceptable if adequate counts are obtained. Slant-hole collimation may be used.
8. A 128×128 or greater acquisition matrix should be used.
9. Use 3° or better angular sampling. The acquisition pixel size should be one third to one half the expected reconstructed resolution. It may be necessary to use a hardware zoom to achieve an appropriate pixel size.

TABLE 2
Radiation Dosimetry in Children (5 Years Old)

Radiopharmaceutical	Administered activity (intravenous)		Organ receiving largest radiation dose		Effective dose	
	MBq	mCi/kg	mGy/kg	rad/mCi	mSv	rem/mCi
^{99m}Tc-HMPAO*	7.4–11.1	0.2–0.3	0.14 (thyroid)	0.52	0.026	0.085
^{99m}Tc-ECD†	7.4–11.1	0.2–0.3	0.083 (bladder wall)	0.31	0.023	0.085

*Data are from ICRP 62, page 13.
†Data are from *Pediatric Nuclear Medicine.* 2nd ed. New York, NY: Springer-Verlag; 1995:576.

Different zoom factors may be used in the *x* and *y* dimensions of a fanbeam collimator.

10. Compared with step-and-shoot technique, continuous acquisition may provide a shorter total scan duration and reduced mechanical wear to the system.
11. Segmentation of data acquisition into multiple sequential acquisitions will permit exclusion of bad data, for example, 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 or the equivalent is indicated to evaluate cerebrovascular reserve in transient ischemic attacks, to evaluate completed stroke or vascular anomalies (e.g., arterial–venous malformation), and to aid in distinguishing vascular from neuronal causes of dementia.

Various protocols have been used, including a split-dose 2-d repeated study and dual-isotope techniques. The 2-d repeated study is simplest and may therefore be preferable. Typically, the challenge portion is performed first. If this has normal results, 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 h). Acetazolamide is a diuretic. The patient should be instructed to void immediately before the beginning of image acquisition. Acquisition and processing are identical to those for a nonacetazolamide study.

Acetazolamide contraindications: Known sulfa allergy is a contraindication (skin rash, bronchospasm, anaphylactoid reaction). Acetazolamide may induce migraine in patients with a history of migraine. Acetazolamide is generally avoided within 3 d of an acute stroke.

Acetazolamide dosage: In adults, give 1,000 mg by slow intravenous push for a typical patient. In children, give 14 mg/kg. Wait 15–20 min after administering acetazolamide before injecting tracer.

Acetazolamide 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

1. Filter all studies in 3 dimensions (*x, y,* and *z*). This can be achieved either by 2-dimensionally prefiltering the projection data or by applying a 3-dimensional postprocessing 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 the highest pixel resolution, that is, 1 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 the 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 3 orthogonal planes. Generate transverse sections relative to a repeatable anatomic orientation (e.g., anterior commissure–posterior commissure 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 healthy individuals and between scans of a single subject obtained at different times. Individual laboratories should obtain or be familiar with a reference database to best interpret patient studies. The Society of Nuclear Medicine (SNM) Brain Imaging Council has developed a publicly available database that is available at brainscans.indd.org.
2. Unprocessed projection images should be reviewed in cinematic display before 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 on film or a paper copy to permit interactive adjustment of contrast, background subtraction, and the color table.
4. Caution must be used in selecting levels of contrast and background subtraction. Noncontinuous 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 on knowledge of a reference 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 the 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 vs. infarct), as well as to the possible effects of atrophy and to partial-volume effects.

7. For epilepsy evaluations, images must be correlated with the relevant electroencephalography 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 "Ethical Clinical Practice of Functional Brain Imaging," a document issued by the SNM Brain Imaging Council and listed in the bibliography of this guideline.

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 or the significance of the abnormality. Many patients will present with nonspecific perfusion patterns that 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 or 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, or poor, including presence of patient movement, deviations from usual laboratory protocol, or other factors, if relevant)
3. Description of abnormalities (including criteria for definition of abnormal—e.g., visual inspection criteria, regions of interest, and comparisons with laboratory databases and reference papers)
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 comorbid conditions, medications, and other diagnostic studies (CT, MRI, electroencephalography). 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 or methodology used is significantly different from that which is typically used (e.g., as described in this guideline), explicitly state the differences in the report. Explicitly describe any limitations of the study.
   d. If a study cannot be interpreted on the basis of well-accepted criteria, include in the clinical report one or more statements similar to the following, as relevant:
      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 [anatomic 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 [anatomic area] could be interpreted as an artifact associated with insufficient resolution or statistical variations.

J. Quality Control

See the SNM Procedure Guideline for General Imaging.

K. Sources of Error

1. The 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 the type and dose of the sedative and the time at which the sedative was administered in relation to the time of tracer injection.
2. Patient motion during data acquisition may produce blurring of image data and may result in artifacts.

IV. ISSUES REQUIRING FURTHER CLARIFICATION

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

V. CONCISE BIBLIOGRAPHY

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VI. DISCLAIMER

The SNM has written and approved this Procedure Guideline as an educational tool designed to promote the cost-effective use of high-quality nuclear medicine procedures in medical practice or in the conduct of research and to assist practitioners in providing appropriate care for patients. The Procedure Guideline should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The guidelines are neither inflexible rules nor requirements of practice and are not intended nor should they be used to establish a legal standard of care. For these reasons, the SNM cautions against the use of this Procedure Guideline in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment about the propriety of any specific procedure or course of action must be made by the physician when considering the circumstances presented. Therefore, an approach that differs from the Procedure Guideline is not necessarily below the standard of care. A conscientious practitioner may responsibly adopt a course of action different from that set forth in the Procedure Guideline when, in his or her reasonable judgment, that course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the Procedure Guideline.

All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of this Procedure Guideline is to assist practitioners in achieving this objective.

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

VII. APPROVAL

This Procedure Guideline was approved by the Board of Directors of the SNM on February 8, 2009.