

The American College of Radiology, with more than 30,000 members, is the principal organization of radiologists, radiation oncologists, and clinical medical physicists in the United States. The College is a nonprofit professional society whose primary purposes are to advance the science of radiology, improve radiologic services to the patient, study the socioeconomic aspects of the practice of radiology, and encourage continuing education for radiologists, radiation oncologists, medical physicists, and persons practicing in allied professional fields.

The American College of Radiology will periodically define new practice guidelines and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice guidelines and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice guideline and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review, requiring the approval of the Commission on Quality and Safety as well as the ACR Board of Chancellors, the ACR Council Steering Committee, and the ACR Council. The practice guidelines and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline and technical standard by those entities not providing these services is not authorized.

2007 (Res. 21)
Effective 10/01/07

ACR PRACTICE GUIDELINE FOR THE PERFORMANCE OF SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) BRAIN PERFUSION AND BRAIN DEATH STUDIES

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such 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 guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment.

Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. 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 these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Single-photon emission computed tomography (SPECT) brain perfusion imaging using lipophilic radiopharmaceuticals that cross the normal blood brain barrier and localize in normal brain tissue is a proven and useful procedure to define the regional distribution of brain perfusion and evaluate a variety of brain abnormalities, and to confirm brain death in appropriate situations.

Application of this guideline should be in accordance with the [ACR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#).

For pediatric considerations see Sections V.A.4 and V.B.3.

II. GOAL

The goal of SPECT brain perfusion imaging is to detect abnormalities in regional cerebral perfusion by producing images of diagnostic quality.

III. INDICATIONS

A. Clinical indications for SPECT brain perfusion studies include, but are not limited to:

1. Detecting and evaluating cerebrovascular disease.
2. Differentiating lacunar from nonlacunar infarctions.
3. Predicting the prognosis of patients with cerebrovascular accidents.
4. Evaluating patients with transient ischemic attacks.
5. Evaluating patients with suspected dementia.
6. Localizing epileptic foci preoperatively.
7. Evaluating symptomatic traumatic brain injury, especially in the absence of computed tomography (CT) and/or magnetic resonance imaging (MRI) findings.
8. Diagnosing encephalitis.
9. Monitoring and assessing vascular spasm following subarachnoid hemorrhage.
10. Mapping of brain perfusion during interventions.
11. Confirming brain death. (Note that these studies can be done with SPECT or with planar technique. See Section VII.G.)

B. For other indications, such as neuropsychiatric disorders and chronic fatigue syndrome, the findings of SPECT brain perfusion imaging have not been fully characterized. In HIV encephalopathy, SPECT brain perfusion imaging can detect organic changes in the brain.

IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the [ACR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#).

V. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for a SPECT brain perfusion study should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should

be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state scope of practice requirements. (2006 - ACR Resolution 35)

A. Radiopharmaceuticals

Either Tc-99m HMPAO (exametazime) or Tc-99m-ECD (ethyl cystine dimer/bicisate) is used.

1. Radiopharmaceutical preparation
 - a. Use fresh generator eluate (<2 hours old) for optimal results with Tc-99m HMPAO.
 - b. Do not use pertechnetate obtained from a generator that has not been eluted for 24 hours or more.
2. Radiopharmaceutical injection
 - a. Tc-99m HMPAO: tracer should be injected no more than 4 hours after reconstitution.
 - b. Tc-99m ECD: tracer should be injected no more than 6 hours after reconstitution.
3. Delay time between injection and imaging
 - a. Tc-99m HMPAO: images should be obtained \geq 90 minutes after injection for best image quality. Images obtained after a 40-minute delay will be interpretable.
 - b. Tc-99m ECD: for best image quality, a minimum delay of 30 minutes is recommended. Images obtained after a 20-minute delay will be interpretable. It is important to standardize delay time and keep it under 3 hours.
 - c. Patients should be instructed to void within 2 hours postinjection to minimize radiation exposure.
4. Dosage
 - a. Adults: 370-1110 MBq (10-30 mCi).
 - b. Children 7.4-11.1 MBq/kg (0.2-0.3 mCi/kg). Minimum dose is 3 mCi.
5. Radiochemical purity determinations should be performed on each vial prior to injection, using the method outlined in the package insert.

B. SPECT Imaging with Acetazolamide

A perfusion study may be performed following the administration of acetazolamide in patients with cerebrovascular disease to evaluate cerebrovascular reserve.

1. Contraindications and adverse reactions
 - a. Known sulfa allergy (skin rash, bronchospasm, and anaphylactic reaction) and advanced liver disease.
 - b. May induce migraine in patients with migraine history.
 - c. Generally avoid within 3 days of acute stroke or recent transient ischemic attack.

2. Protocols

Various protocols have been used. The 2 day technique is simple and preferable. Typically, the acetazolamide 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 to 48 hours).
3. Dosages

Adults should receive 1,000 mg of acetazolamide by slow intravenous (IV) push for the typical patient. The pediatric dose is 14 mg/kg. Wait 15-20 minutes after administering acetazolamide before injecting tracer.
4. Acetazolamide is a diuretic. The patient should be instructed to void immediately before image acquisition begins. Acquisition and processing are identical to those of a nonacetazolamide study.

C. Patient Preparation

Relevant patient data should be obtained for optimal interpretation of the study. The data should include patient history (including any past drug use or trauma), neurologic and psychiatric findings, mental status examination (e.g., Folstein mini-mental examination or other neuropsychological test), results of recent brain imaging studies (e.g., computed tomography [CT], magnetic resonance imaging [MRI]), and current medications, including when they were last taken.

1. Prearrival

Patients should be instructed to avoid caffeine, alcohol, and other drugs known to affect cerebral blood flow (CBF) for at least 24 hours and to avoid smoking cigarettes for at least the day of the test.
2. Preinjection
 - a. Evaluate the patient for his/her ability to cooperate.
 - b. Explain the procedure to the patient, or to the responsible family member or health care proxy.
 - c. Achieve a consistent environment at the time of injection and uptake:
 - i. Place the patient in a quiet, dimly lit room with no direct light source facing the patient's eyes. Whether the eyes are covered or the patient is instructed to open or close his or her eyes should be according to department policy and should be followed consistently.
 - ii. Ensure that the patient is seated or reclining comfortably.
 - iii. Place intravenous access at least 10 minutes prior to injection.

- iv. Instruct the patient not to speak, read, or move prior to, during, and up to 5 minutes postinjection.
 - d. Ensure no movement by the patient.
3. Precautions
 - a. Demented patients must be closely observed at all times.
 - b. Patients with neurologic deficits may require special care.

D. Image Acquisition

1. The patient should void prior to imaging for maximum comfort during the study.
2. The patient should be positioned for maximum comfort. Minor obliquity of head orientation can be corrected in most systems during processing.
3. The patient's head should be positioned in the middle of the field of view with intercanthal line at a 90 degree angle to the axis of rotation and parallel to the horizontal plane. The head should be lightly restrained to facilitate patient cooperation in minimizing motion during acquisition.
4. If sedation is required, it should be given at least 5 minutes after injection of radiopharmaceutical when possible, and preferably just prior to the acquisition of the study.

E. Data Processing

1. Attenuation correction should be performed in all cases unless a specific application or circumstance dictates otherwise. A calculated attenuation correction should be used, if available. If slice-specific attenuation correction software is not available, it is acceptable to review non-attenuation corrected images. The contour should include the scalp and should be defined individually for each transaxial slice.
2. Transaxial data should be reformatted into at least three orthogonal planes. Transverse sections should be generated relative to a repeatable anatomic orientation (e.g., the 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 may be useful.

F. Image Interpretation

1. All studies should be interpreted with the knowledge of all the clinical data and the findings of other morphologic imaging modalities.
2. Images should be viewed on a computer display rather than from film or paper copy, to permit

interactive adjustment of contrast, background subtraction, and color table.

3. Three-dimensional volume renderings may be useful in appreciating overall patterns of disease.
4. The perfusion images should be evaluated in conjunction with available anatomic imaging studies.
5. Images obtained as part of a seizure evaluation should be correlated with the relevant EEG data and clinical observations. The timing of tracer injection relative to observed seizure activity should be known.
6. The raw data should be reviewed in dynamic cine mode for artifacts and patient motion.

G. Brain Death Studies

1. Goal

The goal of cerebral scintigraphy for establishing the presence or absence of brain death is to determine if there is cerebral blood flow.

2. Indications

Cerebral scintigraphy for brain death may be used to confirm the presence or absence of cerebral blood flow in the following situations:

- a. As part of a standardized institutional protocol for establishing brain death.
- b. In situations in which hypothermia or coma caused by barbiturates or other medications impedes evaluation by other modalities.
- c. In other situations in which the referring and interpreting physicians agree that evidence for cerebral blood flow would be helpful.

3. Radiopharmaceuticals

For adults, technetium-99m hexamethyl propylene amine oxime (extametzime) (HMPAO) or technetium-99m ethyl cysteinate dimer (ECD) in an administered activity of up to 30 millicuries (1,110 MBq) is used. Administered activity for children and infants should be reduced based on weight or body surface area; the minimum administered activity is 3 millicuries. Careful adherence to package insert and quality control instructions with HMPAO and ECD is particularly important to ensure optimal image quality. In the past, agents excluded by a normal blood-brain barrier were used with dynamic imaging. This approach is rarely used today.

4. Patient

Prior to setting up the scintillation camera, the team performing the study should evaluate a number of patient factors. If the bed or patient must be moved, the team must avoid placing undue tension or compression on life support lines. Caution must be taken when placing the camera head to avoid compromising any of those lines or transcalvarial cerebrospinal fluid

pressure monitors. Injection of the radiopharmaceutical must be made directly into a vein or through an IV line that is not being used for infusion of vasoactive medications or transfusion of blood. If available, a central venous line is preferable for injection.

5. Examination

Dynamic flow imaging is recommended but is optional. Image acquisition beginning 15-60 minutes after injection for 500,000-1,000,000 counts in the anterior view is recommended. Lateral and posterior images are obtained as needed. SPECT imaging is recommended unless the patient is unstable or has life support equipment that is incompatible with SPECT.

6. Other considerations

The President's Council on Brain Death (1982) determined that of the four examinations available to establish the presence or absence of brain death, two (clinical examination and properly performed four-vessel cerebral angiography) are diagnostic and two (electroencephalography and cerebral scintigraphy) are confirmatory. Thus, one may confirm but not diagnose brain death with cerebral scintigraphy.

A technically adequate study is mandatory for interpretation. Absence of demonstrable radionuclide activity within the brain confirms the clinical diagnosis of brain death.

VI. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Guideline for Communication of Diagnostic Imaging Findings](#).

The report 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 the abnormalities. The report should include the radiopharmaceutical used, the dose injected, the delay period post injection, and any medication administered. In studies other than brain death, the report should also state whether the patient's eyes were open or closed.

VII. EQUIPMENT SPECIFICATIONS

For planar imaging any gamma camera equipped with a low energy, all purpose/general all purpose (LEAP/GAP) or high resolution collimator may be used.

For SPECT imaging any gamma camera equipped with a low-energy high-resolution, ultra-high-resolution, or fan-beam collimator may be used. Either a multiple detector

instrument or a dedicated brain imaging system is preferred to a single-head gamma camera system.

The following is recommended for SPECT imaging:

- A. The smallest radius of rotation possible with appropriate patient safeguards should be used.
- B. High-resolution or ultra-high-resolution collimation is recommended.
- C. Fan-beam or other focused collimators are preferable to parallel-hole collimators because they provide improved resolution and higher count rates. However, care must be taken to ensure that the entire brain is visualized in all projections to avoid the problem of “incomplete” views. Parallel-hole collimation is acceptable if adequate counts are obtained.
- D. A 128 x 128 or greater acquisition matrix is preferred.
- E. Angular sampling of 3 degrees or less is recommended.
- F. Continuous acquisition may provide shorter total scan duration and reduced mechanical wear to the system when compared to a step-and-shoot technique.
- G. Segmentation of data acquisition into multiple sequential acquisitions will permit exclusion of bad data, e.g., removing segments of projection data with patient motion. The scan may be repeated if there is excessive patient motion.

VIII. RADIATION SAFETY

Radiologists, imaging technologists, and all supervising physicians have a responsibility to minimize radiation dose to individual patients, to staff, and to society as a whole, while maintaining the necessary diagnostic image quality. This concept is known as “As Low as Reasonably Achievable (ALARA).”

Facilities, in consultation with the radiation safety officer, should have in place and should adhere to policies and procedures for the safe handling and administration of radiopharmaceuticals, in accordance with ALARA, and must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC), state, and/or other regulatory agencies. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol.

IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

Equipment performance monitoring should be in accordance with the [ACR Technical Standard for Medical Nuclear Physics Performance Monitoring of Nuclear Medicine Imaging Equipment](#).

ACKNOWLEDGEMENT

This guideline was developed according to the process described in the ACR Practice Guidelines and Technical Standards book by the Guidelines and Standards Committee of the Commission on Nuclear Medicine.

Principal Drafter: Michael M. Graham, PhD

Guidelines and Standards Committee

Alice M. Scheff, MD, Co-Chair
James W. Fletcher, MD, Co-Chair
Rodney R. Bowman, MD
Mark F. Fisher, MD
Leonie Gordon, MD
Michael M. Graham, MD, PhD
Ronald L. Korn, MD
Massoud Majd, MD
Sara M. O’Hara, MD
Christopher J. Palestro, MD
Paul D. Shreve, MD
Manuel L. Brown, MD, Chair, Commission

Comments Reconciliation Committee

Jay A. Harolds, MD, Co-Chair
Alan D. Kaye, MD, Co-Chair
Manuel L. Brown, MD
James W. Fletcher, MD
Michael M. Graham, PhD
Paul A. Larson, MD
Lawrence A. Liebscher, MD
Alice M. Scheff, MD
Julie K. Timins, MD

REFERENCES

1. Al-Shammri S, Al-Feeli M. Confirmation of brain death using brain radionuclide perfusion imaging technique. *Med Princ Pract* 2004;13:267-272.

2. Bonetti MG, Ciritella P, Valle G, Perrone E. 99mTc HM-PAO brain perfusion SPECT in brain death. *Neuroradiology* 1995;37:365-369.
3. Camargo EE. Brain SPECT in neurology and psychiatry. *J Nucl Med* 2001;42:611-623.
4. Catafau AM. Brain SPECT in clinical practice. Part I: perfusion. *J Nucl Med* 2001;42:259-271.
5. Conrad GR, Sinha P. Scintigraphy as a confirmatory test of brain death. *Semin Nucl Med* 2003;33:312-323.
6. Devous MD Sr. SPECT functional brain imaging: technical considerations. *J Neuroimaging* 1995;5:S2-S13.
7. Devous MD Sr. SPECT functional brain imaging. In: Kramer EL, Sanger J, eds. *Clinical SPECT Imaging*. New York, NY: Raven Press, Ltd; 1995:97-128.
8. Dougall NJ, Bruggink S, Ebmeier KP. Systematic review of the diagnostic accuracy of 99mTc-HMPAO-SPECT in dementia. *Am J Geriatr Psychiatry* 2004;12:554-570.
9. Ethical clinical practice of functional brain imaging. Society of Nuclear Medicine Brain Imaging Council. *J Nucl Med* 1996;37:1256-1259.
10. Guidelines for the determination of death. Report of the medical consultants on the diagnosis of death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *JAMA* 1981;246:2184-2186.
11. Harding JW, Chatterton BE. Outcomes of patients referred for confirmation of brain death by 99mTc-exametazime scintigraphy. *Intensive Care Med* 2003;29:539-543.
12. Holman BL, Devous MD Sr. Functional brain SPECT: the emergence of a powerful clinical method. *J Nucl Med* 1992;33:1888-1904.
13. Holman BL, Johnson KA, Gerada B, Carvalho PA, Satlin A. The scintigraphic appearance of Alzheimer's disease: a prospective study using technetium-99m-HMPAO SPECT. *J Nucl Med* 1992;33:181-185.
14. Hung JC, Corlija M, Volkert WA, Holmes RA. Kinetic analysis of technetium-99m d, 1-HM-PAO decomposition in aqueous media. *J Nucl Med* 1988;29:1568-1576.
15. Juni JE. Taking brain SPECT seriously: reflections on recent clinical reports in The Journal of Nuclear Medicine. *J Nucl Med* 1994;35:1891-1895.
16. Lu G, Shih WJ, Ryo UY. Findings on Tc-99m HMPAO brain imaging in brain death. *Clin Nucl Med* 1996;21:891-893.
17. Markand ON, Spencer SS, Anderson AR. SPECT in epilepsy. *J Neuroimaging* 1995;5:S23-S33.
18. Masdeu JC, Abdel-Dayem HM, Van Heertum RL. Head trauma: use of SPECT. *J Neuroimaging* 1995;5:S53-S57.
19. Masdeu JC, Brass LM. SPECT imaging of stroke. *J Neuroimaging* 1995;5:S14-S22.
20. Masdeu JC, Van Heertum, RL, Abdel-Dayem, HM. Viral infections of the brain. *J Neuroimaging* 1995;5:S40-S44.
21. Munari M, Zucchetta P, Carollo C, et al. Confirmatory tests in the diagnosis of brain death: comparison between SPECT and contrast angiography. *Crit Care Med* 2005;33:2068-2073.
22. Okuyaz C, Gucuyener K, Karabacak NI, Aydin K, Serdaroglu A, Cingi E. Tc-99m-HMPAO SPECT in the diagnosis of brain death in children. *Pediatr Int* 2004;46:711-714.
23. Spieth M, Abella E, Sutter C, Vasinrapee P, Wall L, Ortiz M. Importance of the lateral view in the evaluation of suspected brain death. *Clin Nucl Med* 1995;20:965-968.
24. Tikofsky RS, Ichise M, Seibyl JP, et al. Functional brain SPECT imaging: 1999 and beyond. In: Freeman LM, ed. *Nuclear Medicine Annual*. Philadelphia, Pa: Lippincott Williams & Wilkins; 1999.
25. Ueda T, Yuh WT. Single-photon emission CT imaging in acute stroke. *Neuroimaging Clin N Am* 2005;15:543-551.
26. Van Heertum FL, Tikofsky RS. *Cerebral Brain SPECT Imaging*. 2nd edition. New York, NY: Raven Press; 1995.
27. Wintermark M, Sesay M, Barbier E, et al. Comparative overview of brain perfusion imaging techniques. *J Neuroradiol* 2005;32:294-314.