Society of Nuclear Medicine Procedure Guideline for Brain Death Scintigraphy

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I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of brain perfusion imaging to assist in confirming the diagnosis of brain death.

II. Background Information and Definitions

The diagnosis of brain death is a clinical diagnosis that is sometimes made with the help of cerebral perfusion scintigraphy. It is important that all physicians be knowledgeable in the clinical requirements for the diagnosis of brain death, especially the need to establish irreversible cessation of all function of the cerebrum and brain stem. Institutions performing scintigraphy for the evaluation of possible brain death should develop clinical guidelines and procedures for the clinical diagnosis that incorporate both clinical evaluations and the integration of ancillary tests such as perfusion scintigraphy.

III. Common Indications

A. Assess brain blood flow in patients suspected of brain death.

IV. Procedure

A. Patient Preparation
   1. No special preparation is necessary.
   2. The patient should have a stable blood pressure, and all correctable major systemic biochemical abnormalities should be addressed.
   3. In some institutions, a tourniquet is placed around the scalp, encircling the head just above the eyebrows, ears, and around the posterior prominence of the skull. The tourniquet can help diminish scalp blood flow, preventing it from being confused with brain blood flow. However, a tourniquet should not be used in patients with a history of head trauma when there is a concern that the tourniquet will exacerbate the injury. A tourniquet may also raise intracranial pressure and, therefore, should not be used unless there is adequate monitoring of intracranial pressure or there is little reason to expect an elevation of intracranial pressure.
   4. Patients should be normally ventilated to prevent changes in cerebral blood flow that may be caused by hyperventilation.

B. Information Pertinent to Performing the Procedure
   1. History of head trauma or central nervous system (CNS) injury should be obtained. Trauma or focal CNS ischemia or infection may cause abnormalities in blood flow that may complicate image interpretation.
   2. It should be determined whether the patient can be positioned as needed for brain perfusion imaging. Anterior or posterior images should be properly aligned so that symmetry of blood flow to both sides of the head and superior sagittal sinus activity can be assessed.
   3. Care should be taken to note whether the patient has recently received barbiturates. At high levels, these agents may decrease cerebral blood flow.

C. Precautions
   None

D. Radiopharmaceutical
   Several ^{99m}Tc-labeled agents may be used, including:
   1. ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD)
   2. ^{99m}Tc-hexamethylpropylene amine oxime (^{99m}Tc-HMPAO)
   3. ^{99m}Tc-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA)

   Although brain-specific tracers such as ^{99m}Tc-

Radiation Dosimetry in Adults

Radiopharmaceuticals	Administered Activity MBq (mCi)	Organ Receiving the Largest Radiation Dose MGy/MBq (rad/mCi)	Effective Dose MSv/MBq (rem/mCi)
^{99m}Tc-DTPA[1]	555–740 intravenously (15–20)	0.065 Bladder wall (0.24)	0.0063 (0.023)
^{99m}Tc-HMPAO[2]	370–1,110 intravenously (10–30)	0.034 Kidneys (0.0126)	0.0093 (0.034)
^{99m}Tc-ECD[3]	370–1,110 intravenously (10-30)	0.073 Bladder wall (0.27)	0.011 (0.042)

[1] International Commission on Radiological Protection and Measurements. *Radiation Dose to Patients from Radiopharmaceuticals*. ICRP report no. 53. London, UK: ICRP; 1988:188.
[2] International Commission on Radiological Protection and Measurements. *Radiological Protection in Biomedical Research*. ICRP report no. 62. London, UK: ICRP; 1993:13.
[3] Oak Ridge Institute for Science and Education. *Radiation Dose Estimates for Radiopharmaceuticals*. Oak Ridge, TN: Radiation Internal Dose Information Center. Available at: www.orau.gov/ehsd/DOSETABLES.doc. Accessed Feb.13, 2003.

HMPAO and ^{99m}Tc-ECD are increasing in popularity, there is no clear evidence they are more accurate than nonspecific agents. Brain-specific agents are preferred by some institutions, because their interpretation is far less dependent on the quality of the bolus and because delayed images are usually definitive for the presence or absence of cerebral blood flow.

The Brain Imaging Council of the Society of Nuclear Medicine believes that although individual laboratories may have used and may continue to use agents such as DTPA, glucoheptonate, and pertechnetate (with perchlorate blockade), these are much less favorable than HMPAO and ECD for assessment of cerebral perfusion.

E. Image Acquisition

Flow images should be acquired. They are essential for interpretation of studies using non-brain-binding agents such as ^{99m}Tc-DTPA. In studies using brain-specific agents, such as ^{99m}Tc-HMPAO and ^{99m}Tc-ECD, lack of visualization of the brain on delayed images could conceivably be caused by improper preparation or instability of the radiopharmaceutical. Flow images will help to confirm lack of brain blood flow when the brain is not visualized on delayed images using ^{99m}Tc-HMPAO and ^{99m}Tc-ECD.

1. Instrumentation
   a. Gamma camera with field of view large enough to image entire head and neck.
   b. Low-energy high-resolution (LEHR) or ultra-high resolution (UHR) collimator.
   c. 15%–20% energy window centered around 140 keV.
2. Flow images are acquired at the time of tracer injection.
   a. 1–3 s per frame for at least 60 s. Flow images should start before the arrival of the bolus in the neck and end well after the venous phase.
   b. Use of high-resolution or UHR collimation is recommended. As a general rule, use the highest resolution collimation available.
3. Static images
   a. If a non-brain-binding agent, such as ^{99m}Tc-DTPA, is used, static images are acquired immediately for 5 min in anterior, right lateral, left lateral, and, if possible, posterior projections for approximately 5 min per view. Zooming or magnification may be helpful, particularly in pediatric cases.
   b. For brain-specific agents, planar and SPECT images should be obtained after at least 20 min. Images should be obtained in anterior, right lateral, left lateral, and, if possible, posterior projections.
4. When using brain-specific agents, such as ^{99m}Tc-HMPAO and ^{99m}Tc-ECD, SPECT images may be obtained in addition to flow and planar images as described above. SPECT allows better visualization of perfusion to the posterior fossa and brain stem structures.

Radiation Dosimetry in Children (5 Years Old; Normal Renal Function)

Radiopharmaceuticals	Administered Activity			Organ Receiving the Largest Radiation Dose MGy/MBq (rad/mCi)	Effective Dose MSv/MBq (rem/mCi)
	MBq/kg Dose (mCi/kg)	Minimum Dose MBq (mCi)	Maximum Dose MBq (mCi)		
^{99m}Tc-DTPA[1]	7.4 intravenously (0.2)	370 (10)	740 (20)	0.17 Bladder wall (0.63)	0.017 (0.063)
^{99m}Tc-HMPAO[2]	11.1 intravenously (0.3)	185 (5)	740 (20)	0.14 Thyroid (0.52)	0.026 (0.096)
^{99m}Tc-ECD[3]	11.1 intravenously (0.3)	185 (5)	740 (20)	0.083 Bladder wall (0.31)	0.023 (0.085)

[1] International Commission on Radiological Protection and Measurements. *Radiation Dose to Patients from Radiopharmaceuticals*. ICRP report no. 53. London, UK: ICRP; 1988:188.
[2] International Commission on Radiological Protection and Measurements. *Radiological Protection in Biomedical Research*. ICRP report no. 62. London, UK: ICRP; 1993:13.
[3] Oak Ridge Institute for Science and Education. *Radiation Dose Estimates for Radiopharmaceuticals*. Oak Ridge, TN: Radiation Internal Dose Information Center. Available at: www.orau.gov/ehsd/pedose.doc. Accessed Feb. 13, 2003.

However, SPECT is rarely, if ever, used in these patients who are often unstable and on life support equipment, which may be incompatible with SPECT acquisition.

a. 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).
b. LEHR or fanbeam collimators are preferred when SPECT images will be acquired. As a general rule, use the highest resolution collimation available.
c. Use the smallest possible radius of rotation.
d. A 128×128 or greater acquisition matrix is preferred.
e. Angular sampling of 3° or better is preferred. 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 with in-plane and axial dimensions of a fanbeam collimator.
f. The time per stop and number of counts acquired for the study will depend on the amount of tracer activity in the brain and the specific camera being used. It is suggested that the number of seconds per stop be similar to that used on your equipment for acquiring other brain SPECT studies.
g. 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
None
G. Processing: SPECT
1. Filter studies in 3 dimensions. This can be achieved either by 2-dimensionally prefiltering the projection data or by applying a 3-dimensional postfilter to the reconstructed data.
2. Low-pass (e.g., Butterworth) filters should be used. Resolution recovery or spatially varying the filters should be used with caution, however; they may produce artifacts.
3. Always reconstruct the *entire* brain. Use care not to exclude the cerebellum or vertex.
4. Reconstruct data at highest pixel resolution (i.e., 1 pixel thick). If slices are to be summed, this should be done only after reconstruction and oblique reorientation (if performed).

H. Interpretation Criteria
1. For studies using brain-specific agents:

a. Flow images in brain death are characterized by a lack of flow to the middle cerebral artery, the anterior cerebral artery, and the posterior cerebral artery. This often results in a lack of a "blush" of activity in the middle of the head during flow images. Keep in mind that the external carotid artery will likely remain patent and there will be some flow to the scalp, which can be mistaken for brain flow in some instances. Another important sign in brain death is lack of tracer activity in the superior sagittal sinus during the venous phase of the flow study.
b. Flow images are assessed for blood flow to the brain.
   (1) Anterior views are preferred for imaging blood flow. The head should be viewed straight on to allow for comparison of right and left carotid flow.
   (2) Tracer flow should be observed from the level of the carotids to the skull vertex. In the anterior position, the right and left middle cerebral arteries appear along the lateral aspects of the skull. The anterior cerebral arteries appear midline and appear as 1 vessel.
   (3) In brain death, blood flow superior to the circle of Willis circulation is completely absent. There may be an accompanying blush of activity in the region of the nose ("hot nose sign"). Care must be taken to distinguish external carotid circulation to the scalp from internal carotid circulation to the brain.
   (4) The superior sagittal sinus is often noted during the venous phase of blood flow in patients with intact blood flow to the brain. However, low-level sagittal sinus activity can come from the scalp. If no internal carotid flow or CNS perfusion is seen on the flow study and minimal sagittal sinus activity is noted, these findings should be noted and a note of caution regarding the accuracy of the interpretation included in the report.
   (5) In cases of head trauma, hyperemic blood flow to injured scalp structures may mimic brain blood flow or superior sagittal sinus activity.
   (6) CSF shunts and intracranial pressure transducers can cause hyperemia resulting in increased scalp flow, possibly causing a false-negative flow study. Disruptions in the skull and scalp, as well as pressure on the portion of the scalp resting on a hard surface, can produce a relatively photopenic area on the flow study, falsely suggesting diminished flow.
c. Delayed planar or SPECT images should demonstrate no tracer uptake in the brain for the diagnosis of brain death to be made. For SPECT studies, unprocessed projection images should be reviewed in cinematic display before viewing of tomographic sections. Projection data should be assessed for target-to-background ratio and other potential artifacts. Inspection of the projection data in sinogram form may also be useful. The role and use of SPECT imaging is unclear. Both cerebral hemispheres and the posterior fossa (cerebellum) should be evaluated for a complete study. Therefore, if performing planar scintigraphy an anterior-posterior or posterior-anterior view, separating left and right hemispheres and at least 1 lateral view to distinguish the cerebral flow from that of the cerebellum are commonly needed.
d. Images viewed on a computer screen rather than from film or paper copy permit interactive adjustment of contrast, background subtraction, and color table.
e. Grayscale is preferred to color tables. At very low levels of activity, color tables usually designed for viewing near-normal activity may under-represent low activity, causing a false-positive study.

2. For studies using non-brain-binding agents
   a. Delayed images using agents that are not brain specific should not demonstrate superior sagittal sinus activity in patients with brain death. Another finding that may be present in patients with brain death is the "halo" sign. This is a photopenic defect caused by compression of scalp blood flow that may be seen when the patient's head is resting on a firm object, such as an imaging table.

I. Reporting
   1. Reports should include the tracer used and basic imaging information, such as the acquisition of SPECT and/or planar images. Flow images should be reported in a separate paragraph.
   2. Reports should describe the extent and severity of brain perfusion deficits. If brain-specific agents are used, specific mention of perfusion to the posterior fossa and brain stem may be reported. Because this study is used in combi-

nation with other tests and physical exam findings, the final impression of a positive study should state that the study is "consistent with brain death" rather than "demonstrates brain death."

3. Severely decreased brain perfusion is often progressive. If there is a small amount of remaining perfusion, consider recommending a repeat study in 24 h.

J. Quality Control
   1. If using brain-specific agents, quality control of labeling and stability of the compound is essential to prevent false-positive results. Poor radiopharmaceutical labeling or stability would result in minimal concentration of tracer in the brain. This could be falsely interpreted as lack of cerebral perfusion.
   2. See *Society of Nuclear Medicine Procedure Guideline for General Imaging.*

K. Sources of Error
   1. Improper labeling of brain-specific radiopharmaceuticals or injection of the wrong radiopharmaceutical can result in false-positive studies as described in section J.1.
   2. Drainage of blood from the scalp into the superior sagittal sinus may cause a false-negative flow study.
   3. Hyperemic scalp structures may result in false-negative flow studies if non-specific brain agents are used.
   4. Infiltration of tracer at injection site may cause a false-positive study if the entire dose is infiltrated and not available to the vascular space. Absence of activity in the carotid vessels on flow images suggests complete infiltration of the dose.

V. Issues Requiring Further Clarification

A. The relative accuracies of brain-specific and nonspecific agents.
B. The importance of SPECT imaging.
C. The value of brain-specific agents for the detection of small areas of brain perfusion, such as in the posterior fossa. Will this increased sensitivity for small areas of perfusion change the ultimate prognosis?
D. The influence of open fontanels in small children upon the accuracy of flow studies.

VI. Concise Bibliography

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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.