THE SNM PRACTICE GUIDELINE FOR BRAIN DEATH SCINTIGRAPHY V2.0

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate 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 Society of Nuclear Medicine (SNM) 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 of available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

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 care.
medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

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. GOALS

The goal of this guideline is to describe some of the elements common to optimal performance of Brain Death Scintigraphy.

III. DEFINITIONS

See also SNM Procedure Guideline for General Imaging

The diagnosis of brain death is a clinical diagnosis that is sometimes confirmed with cerebral perfusion scintigraphy \((1,2)\). It is important that all physicians be knowledgeable in the clinical requirements for the diagnosis of brain death, especially the need to establish reversible cessation of all function of the cerebrum and brain stem \((3)\). 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 \((4)\).

IV. COMMON CLINICAL INDICATIONS

Assessment of brain death is not addressed in the American College of Radiology (ACR) Appropriateness Criteria at the time of the revision of this guideline.

Indications for Brain Death Scintigraphy include, but are not limited to the following \((5-12)\):


The subset of clinical cases where this study may be helpful includes:

A. Where clinical assessment and electro-encephalography are less reliable in diagnosing brain death due to presence of medical conditions such as severe hypothermia, coma caused by barbiturates, electrolyte or acid-base imbalance, endocrine disturbances, drug intoxication, poisoning and neuromuscular blockade.

B. In patients who are being considered as possible organ donors \((13)\).
C. Document lack of blood flow for family members.

V. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL (in the United States)

Refer to Section V. of the SNM Procedure Guideline for General Imaging.

VI. PROCEDURE/SPECIFICATIONS OF THE EXAMINATION

A. Patient Preparation

1. The patient should have a stable blood pressure and all correctable major systemic biochemical abnormalities should be addressed. Patients may be unstable, making transportation and SPECT imaging logistically difficult and hazardous for the patient. Before moving the patient, the relative risks and benefits of imaging away from the patient’s room, such as with SPECT or SPECT/CT, should be weighed.

2. In some institutions a tourniquet is placed, 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.

3. 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 CNS injury should be obtained. Trauma or focal CNS ischemia or infection may cause abnormalities in blood flow that may complicate image interpretation. Clinical findings should also be reviewed, such as the results of neurological tests and any other testing that may support the diagnosis of brain death.

2. It should be determined if 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 if the patient has recently received barbiturates. At high levels, these agents may decrease cerebral blood flow (14).

4. Additional brain imaging studies should be reviewed, if available.
C. Precautions

None

D. Radiopharmaceutical

See also SNM Procedure Guideline for Use of Radiopharmaceuticals.

Several $^{99m}$Tc-labeled agents may be used (15, 16, 17), including:

1. $^{99m}$Tc-bicisate (ECD; ethyl cysteinate dimer)
2. $^{99m}$Tc-exametazime (HMPAO; hexamethylpropylene amine oxime)
3. $^{99m}$Tc-pentetate (DTPA; diethylenetriaminepentaacetic acid)

While brain-specific tracers such as $^{99m}$Tc-HMPAO and $^{99m}$Tc-ECD are increasing in popularity, there is no clear evidence they are more accurate than non-specific agents. Brain specific agents are preferred by some institutions as their interpretation is far less dependent on the quality of the bolus and delayed images are usually definitive for the presence or absence of cerebral blood flow. They also offer the advantage of evaluating regional brain tissue perfusion and hence brain viability (18) as opposed to $^{99m}$Tc-DTPA which cannot cross the blood-brain barrier and therefore provides only low-resolution vascular flow information.

In adults, up to 30 millicuries (1,110 MBq) administered activity may be used. Administered activity for children should be determined based on body weight and should be as low as reasonably achievable for diagnostic image quality. The typical dose in children is 11.1 MBq/kg (0.3 mCi/kg); minimum dose of 148 MBq (4 mCi).

The Brain Imaging Council of the Society of Nuclear Medicine feels that while individual laboratories may have used and may continue to use agents such as DTPA, glucoheptonate, and pertechnetate, these are less commonly used than HMPAO and ECD for assessment of cerebral perfusion (19).

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, poor (or suboptimal) 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. Flow images are acquired at the time of tracer injection.

   a. A 15 - 20% energy window centered around 140 keV is set prior to the start of
imaging.

b. Flow images are obtained at 1-3 seconds per frame for at least 60 seconds.

c. The acquisition should start before or at the time of injection, to ensure imaging begins before the bolus reaches the carotid arteries, and end well after the venous phase.

2. Static images

a. If a non-brain binding agent, such as $^{99m}$Tc-DTPA is used, static images are acquired in anterior (and posterior, if helpful) and one lateral view for 500,000 to 1,000,000 counts per view. Zooming or magnification may be helpful, particularly in pediatric cases.

b. For brain-specific agents, images should be obtained after approximately 20 minutes. Planar images should be obtained in anterior, right lateral, left lateral and, if possible, posterior projections if SPECT is not feasible (20).

3. SPECT Imaging

a. 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 (19); however, SPECT is rarely, if ever, used in patients that are unstable and on life support equipment, which is often incompatible with SPECT acquisition.

b. 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 ($5 \times 10^6$ total counts or more are desirable).

c. The smallest radius of rotation possible with appropriate patient safeguards should be used (21)

d. High-resolution or ultra-high-resolution collimation is recommended (21)

e. Low energy high resolution or ultra-high resolution collimators may be used. 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. When parallel-hole collimation is used, care should be taken to ensure adequate counts are obtained.
e. A 128 x 128 or greater acquisition matrix is preferred. Camera zoom should be set to produce a pixel size of 3.5mm or less.

f. Continuous acquisition may provide shorter total scan duration when compared to a step-and-shoot technique. When continuous acquisition is used, it is very important that angular sampling of 3 degrees or less be used. 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 fan-beam collimator.

g. 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.

h. 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 shoulders.

i. 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 also be repeated if there is excessive patient motion.

F. Interventions

None

G. Processing - SPECT

1. Filter studies in 3 dimensions. 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 be used. Resolution recovery or spatially varying the filters should be used with caution, however, as they may produce artifacts.

3. Always reconstruct the entire brain. Use care not to exclude the cerebellum or vertex (20).

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).
H. Interpretation Criteria

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. According to evidence-based review, radionuclide studies remain an acceptable corroborative test (12).

A technically adequate study is mandatory for interpretation. The absence of demonstrable radionuclide activity within the brain is consistent with the diagnosis of brain death, but not sufficient by itself to make this diagnosis, and should be correlated with other findings.

Images viewed on a computer screen rather than on film or paper copy permit interactive adjustment of contrast, background subtraction and color table.

1. For studies using brain-specific agents:

   a. Flow images are assessed for blood flow to the brain.

      i. 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.

      ii. 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 course from the midline to the lateral aspects of the skull. The anterior cerebral arteries appear midline and appear as one vessel.

      iii. In brain death, intracranial blood is completely absent. There may be an accompanying blush of activity apparently in the region of the nose on anterior views (“hot nose sign”) which is more likely to represent re-routed blood flow to the region of the brainstem or cervical region of the spinal cord (22). Care must be taken to distinguish external carotid circulation to the scalp from internal carotid circulation to the brain (23).

      iv. 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 (24).

      v. In cases of head trauma, hyperemic blood flow to injured scalp structures may mimic brain blood flow or superior sagittal sinus activity (25).
vi. 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.

b. Delayed planar or SPECT images should demonstrate no tracer uptake in the brain for the diagnosis of brain death to be made in studies using brain-specific agents. For SPECT studies, unprocessed projection images should be reviewed in cinematic display prior to 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. Both cerebral hemispheres and the posterior fossa (cerebellum) should be evaluated for a complete study. Therefore, if performing planar scintigraphy an AP or PA view, separating left and right hemispheres, and at least one lateral view to distinguish the cerebral flow from that of the cerebellum are commonly needed (15, 18, 26).

c. Gray scale 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:

Delayed images using agents that are not brain specific may show superior sagittal sinus activity even in the presence of brain death in as many as 50% of patients (24). If superior sagittal sinus activity is not seen, however, it helps confirm the lack of cerebral perfusion.

VII. DOCUMENTATION AND REPORTING

See also SNM Procedure Guideline for General Imaging

A. Reports should include the tracer used, injected activity, and basic imaging information, such as whether flow, planar, and/or SPECT images were obtained.

B. A brief history and description of clinical findings that support the diagnosis of brain death should be included.

C. Reports should describe the extent and severity of brain perfusion deficits.

D. 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 combination 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”.
E. Severely decreased brain perfusion is often progressive. If there is a small amount of remaining perfusion, consider recommending a repeat study (17, 28).

VIII. EQUIPMENT SPECIFICATION

A. Instrumentation

1. A gamma camera with a field of view large enough to image the entire head and neck (a small field of view portable camera with a diverging collimator to include the entire head and neck in the image may also be used).

2. Low energy, High Resolution (LEHR) or Ultra-High Resolution (UHR) collimator.

3. For SPECT imaging, a multiple detector instrument or a dedicated brain imaging system is preferred to a single-head gamma camera system. A SPECT/CT camera may also be utilized, if available.

IX. QUALITY CONTROL AND IMPROVEMENT

A. See SNM Procedure Guideline for General Imaging.

B. Quality Control

1. If using brain-specific agents, high radiochemical purity and stability of the radiopharmaceutical are essential to prevent false positive results. Substandard radiochemical purity, e.g., due to improper preparation or instability, would result in reduced concentration of tracer in the brain. This could be falsely interpreted as lack of cerebral perfusion.

2. Intravenous access must be definitely established so that the flow bolus is compact. Infiltration of the injected dose or a prolonged bolus makes evaluation of the flow phase difficult.

C. Sources of error

1. Substandard radiochemical purity of brain-specific radiopharmaceuticals or injection of the wrong radiopharmaceutical can result in false-positive studies as described above in section IX.B.1.

2. Tracer can accumulate in the superior sagittal sinus from a number of sources. Superior sagittal sinus activity may be mistaken as a sign of cerebral arterial flow (24).

3. Hyperemic scalp structures may result in false-negative flow studies if non-specific brain agents are used.
4. Infiltration of tracer at the 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.

5. Retained radioactivity from a previous study using $^{99m}$Tc-HMPAO or $^{99m}$Tc-ECD may impede a correct diagnosis for a repeat study on the same day \((17, 29)\).

D. Issues Requiring Further Clarification

4. The relative accuracies of brain-specific and non-specific agents.

5. The clinical necessity of SPECT imaging.

6. 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 residual perfusion change the ultimate prognosis?

4. The influence of open fontanels in small children upon the accuracy of flow studies.

X. RADIATION SAFETY IN IMAGING

*See also Section IX of SNM Procedure Guideline for General Imaging.*

**Radiation Dosimetry - Adults**

<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>Administered Activity MBq (mCi)</th>
<th>Organ Receiving the Largest Radiation Dose mGy/MBq (rad/mCi)</th>
<th>Effective Dose mSv/MBq (rem/mCi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc-DTPA (30)</td>
<td>555-740 i.v. (15 - 20)</td>
<td>0.065 Bladder wall (0.24)</td>
<td>0.0063 (0.023)</td>
</tr>
<tr>
<td>$^{99m}$Tc-HMPAO (31)</td>
<td>370-1110 i.v. (10-30)</td>
<td>0.034 Kidneys (0.0126)</td>
<td>0.0093 (0.034)</td>
</tr>
<tr>
<td>$^{99m}$Tc-ECD</td>
<td>370-1110 i.v. (10-30)</td>
<td>0.05 Bladder wall (0.18)</td>
<td>0.0077 (0.028)</td>
</tr>
</tbody>
</table>
Radiation Dosimetry - Children
(5 year old; Normal Renal Function)

<table>
<thead>
<tr>
<th>Radiopharmaceuticals</th>
<th>Administered Activity</th>
<th>Organ Receiving the Largest Radiation Dose</th>
<th>Effective Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MBq/kg (mCi/kg)</td>
<td>Minimum Dose MBq (mCi)</td>
<td>Maximum Dose MBq (mCi)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-DTPA (30)</td>
<td>7.4 i.v.</td>
<td>370 (10)</td>
<td>740 (20)</td>
</tr>
<tr>
<td></td>
<td>(0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-HMPAO (31)</td>
<td>11.1 i.v.</td>
<td>185 (5)</td>
<td>740 (20)</td>
</tr>
<tr>
<td></td>
<td>(0.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Tc-ECD (32)</td>
<td>11.1 i.v.</td>
<td>185 (5)</td>
<td>740 (20)</td>
</tr>
<tr>
<td></td>
<td>(0.3)</td>
<td></td>
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</tbody>
</table>

The Pregnant or Potentially Pregnant Patient

$^{99m}$Tc-DTPA: Dose estimates to the fetus were provided by Russell et al. (33). Information about possible placental crossover of this compound was included in the calculations.

<table>
<thead>
<tr>
<th>Stage of Gestation</th>
<th>Fetal Dose mGy/MBq (rad/mCi)</th>
<th>Fetal Dose mGy (rad)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>0.012 (0.044)</td>
<td>6.7-8.9 (0.67-0.89)</td>
</tr>
<tr>
<td>3 months</td>
<td>0.0087 (0.032)</td>
<td>4.8-6.4 (0.48-0.64)</td>
</tr>
<tr>
<td>6 months</td>
<td>0.0041 (0.015)</td>
<td>2.3-3.0 (0.23-0.30)</td>
</tr>
<tr>
<td>9 months</td>
<td>0.0047 (0.017)</td>
<td>2.6-3.5 (0.26-0.35)</td>
</tr>
</tbody>
</table>

$^{99m}$Tc-HMPAO: Dose estimates to the fetus were provided by Russell et al. (33). No information about possible placental crossover of this compound was available.
Table 1. Fetal Dose

<table>
<thead>
<tr>
<th>Stage of Gestation</th>
<th>Fetal Dose</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mGy/MBq (rad/mCi)</td>
<td>mGy (rad)</td>
</tr>
<tr>
<td>Early</td>
<td>0.0087 (0.032)</td>
<td>3.2-9.7 (0.32-0.97)</td>
</tr>
<tr>
<td>3 months</td>
<td>0.0067 (0.025)</td>
<td>2.5-7.4 (0.25-0.74)</td>
</tr>
<tr>
<td>6 months</td>
<td>0.0048 (0.018)</td>
<td>1.8-5.3 (0.18-0.53)</td>
</tr>
<tr>
<td>9 months</td>
<td>0.0036 (0.013)</td>
<td>1.3-4.0 (0.13-0.40)</td>
</tr>
</tbody>
</table>

\[^{99m}\text{Tc-ECD}\): No fetal dosimetry is available presently.

The Breastfeeding Patient

ICRP Publication 106, Appendix D suggests that no interruption of breastfeeding is needed for administrations of \[^{99m}\text{Tc-DTPA}, ^{99m}\text{Tc-HMPAO}\] or \[^{99m}\text{Tc-ECD}\].

XI. ACKNOWLEDGEMENTS

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XIII. BOARD OF DIRECTORS APPROVAL DATES

Version 1.0 January 25, 2003