SPECIAL CONTRIBUTIONS

SNMMI Procedure Standard/EANM Practice Guideline for Amyloid PET Imaging of the Brain 1.0

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PREAMBLE

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is an international scientific and professional organization founded in 1954 to promote the science, technology, and practical application of nuclear medicine. Its 18,000 members are physicians, technologists, and scientists specializing in the research and practice of nuclear medicine. In addition to publishing journals, newsletters, and books, the SNMMI also sponsors international meetings and workshops designed to increase the competencies of nuclear medicine practitioners and to promote new advances in the science of nuclear medicine. The European Association of Nuclear Medicine (EANM) is a professional nonprofit medical association that facilitates communication worldwide between individuals pursuing clinical and research excellence in nuclear medicine. The EANM was founded in 1985.

The SNMMI/EANM will periodically define new standards/guidelines for nuclear medicine practice to help advance the science of nuclear medicine and to improve the quality of service to patients. Existing standards/guidelines will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated. Starting February 2014, the SNMMI guidelines have been referred to as procedure standards. Any practice guideline or procedure guideline published before that date is now considered an SNMMI procedure standard.

Each standard/guideline, representing a policy statement by the SNMMI/EANM, has undergone a thorough consensus process in which it has been subjected to extensive review. The SNMMI/EANM recognizes that the safe and effective use of diagnostic nuclear medicine imaging requires specific training, skills, and techniques, as described in each document.

The EANM and SNMMI have written and approved these standards/guidelines to promote the use of nuclear medicine procedures with high quality. These standards/guidelines are intended to assist practitioners in providing appropriate nuclear medicine 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 SNMMI/EANM cautions against the use of these standards/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 medical professionals taking into account the unique circumstances of each case. Thus, there is no implication that an approach differing from the standards/guidelines, standing alone, is 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 standards/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 standards/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 standards/guidelines will not ensure 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 standards/guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Extracellular deposition of Aβ peptides (or plaques) is one of the pathologic hallmarks of Alzheimer disease (AD) (1). The recent development of molecular imaging tracers that bind to Aβ plaques in the brain has enabled in vivo detection of Aβ plaque deposition using PET. Noninvasive detection of Aβ deposition may potentially contribute to better diagnosis and management...
of patients with cognitive decline suspected of having neurodegenerative disorders. Additionally, confirmation of the presence of Aβ deposition among subjects and monitoring of changes in Aβ deposition may become critical in therapeutic interventions that are specifically designed to remove Aβ deposits from the brain. As of 2015, 3 compounds had been approved for imaging Aβ plaques by the U.S. Food and Drug Administration and the European Medicines Agency: 18F-florbetapir (Amyvid; Eli Lilly), 18F-flutemetamol (Vizamyl; GE Healthcare), and 18F-florbetaben (NeuraCeq; Piramal Pharma).

AD is the most common form of dementia. It is a neurodegenerative disease characterized by a constellation of clinical symptoms ranging from declines in short-term memory or executive function to behavioral changes, loss of language, alogia, impaired psychosocial function, and eventually death. The hallmarks of the disease have been classically defined by neuropathologic changes including the formation of abundant Aβ plaques and neurofibrillary tangles of phosphorylated tau protein. Such protein aggregations are hypothesized to provoke or result from other pathologic processes observed in AD, including inflammation, synaptic dysfunction, neuronal disconnection, and neuronal loss. However, the exact pathogenesis of AD and cascades of pathologic changes are still a matter of intense debate and investigation.

Recently the National Institute on Aging–Alzheimer Association and the Consortium to Establish a Registry for Alzheimer Disease, as well as the International Working Group, published updated consensus guidelines for the neuropathologic assessment of AD (2–4). These guidelines define AD as a clinicopathologic entity, instead of neuropathologic disease confirmed at autopsy, with a set of clinical signs and symptoms of cognitive and behavioral changes that are typical of patients who have substantial AD neuropathologic changes. The National Institute on Aging–Alzheimer Association consensus guidelines describe AD as a continuum of pathologic processes ranging from preclinical AD and mild cognitive impairment (MCI) to dementia. This has set the stage for biomarkers, including imaging biomarkers to play a role in defining and diagnosing the various time points (stages) along the AD continuum.

Preclinical AD is defined as the stage of the disease at which a series of pathologic events, including Aβ buildup, is occurring in the brain before the onset of significant and clinically detectable symptoms.

MCI is marked by clinical symptoms of memory or other cognitive problems greater than normal for age and education. These symptoms are mild enough not to interfere with independent and instrumental activities of daily living such as dressing, eating, and caring for personal hygiene. It is important to note that MCI is a heterogeneous entity, that not everyone with MCI has AD, and that MCI patients may or may not progress to dementia. However, the risk of conversion to clinically manifest dementia is significantly increased in MCI, and MCI can thus be considered a risk factor for the development of AD dementia.

Other patients who may benefit from an amyloid imaging biomarker include those with probable AD dementia (5,6) and those with possible AD dementia (7).

II. GOALS

The goal of this standard/guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of brain PET imaging that depicts β-amyloid (Aβ) deposition in the brain (referred to as amyloid PET hereafter).

III. COMMON CLINICAL INDICATIONS

Appropriate-use criteria for amyloid PET have been published recently by the SNMMI and Alzheimer’s Association joint task force (5–10). The appropriate-use criteria emphasize that amyloid PET is currently most likely to be helpful when the patient has objectively confirmed cognitive impairment, when the cause of cognitive impairment remains uncertain after a comprehensive evaluation by a dementia expert, when the differential diagnosis includes AD dementia, and when knowledge of the presence or absence of Aβ pathology is expected to increase diagnostic certainty or alter patient management.

Dementia experts are defined as physicians trained and board-certified in neurology, psychiatry, or geriatric medicine who devote a substantial proportion (>25%) of patient contact time to the evaluation and care of adults with acquired cognitive impairment or dementia, including probable or suspected AD (8).

The use of amyloid PET is considered appropriate when any of the following is true: the patient has persistent or progressive unexplained MCI; the core clinical criteria for possible AD are satisfied but there is an unclear clinical presentation—either an atypical clinical course or an etiologically mixed presentation; or the patient has progressive dementia and the age of onset was atypically early (usually defined as ≤65 y).

The use of amyloid PET is considered inappropriate when any of the following is true: the patient meets the core clinical criteria for probable AD and had a typical age of onset, there is a need to determine the severity of dementia, the patient is asymptomatic and either has a family history of AD or has been shown to carry the ε4 allele of apolipoprotein E, the patient has a cognitive complaint that has not been confirmed on clinical examination, a test in lieu of genotyping is needed for a patient who is a suspected autosomal dominant mutation carrier, the patient is asymptomatic, or the imaging is to be performed for nonmedical reasons (e.g., legal, insurance coverage, or employment screening).

The above appropriate-use criteria have not been validated for patient outcome or for use of possible future anti-Aβ therapies, and further health services research is necessary to determine effective clinical use of amyloid PET.

IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

Amyloid PET examinations should be performed by, or under the supervision of, a physician specialized in nuclear medicine and certified by accrediting boards. Physicians who interpret amyloid PET results should also complete appropriate training programs provided by the manufacturers of approved radiotracers.

B. Technologist

Amyloid PET examinations should be performed by qualified registered or certified nuclear medicine technologists. See Performance Responsibility and Guidelines for the Nuclear Medicine Technologist for further details.

V. PROCEDURE/SPECIFICATIONS OF THE EXAMINATION

See also the SNMMI Procedure Standard on General Imaging. As of the end of 2014, 18F-florbetapir, 18F-flutemetamol, and 18F-florbetaben had been approved by the U.S. Food and Drug
Administration and the European Medicines Agency for amyloid PET examinations. Although these radiotracers share a common imaging target and similar imaging characteristics, amyloid tracers can differ in their tracer kinetics, specific binding ratios, and optimal imaging parameters (11).

A. Nuclear medicine study request

The nuclear medicine imaging facility should check with its local nuclear pharmacy provider as to the availability of the radiotracer before scheduling the examination. Advanced notice may be required for tracer delivery.

The study requisition should include clinical information about the patient to justify the study and to allow coding of the examination or study, information about the ability of the patient to cooperate with the test, and information about current medications in case mild sedation is necessary. It is also helpful to know if the patient needs to be accompanied by a guardian.

B. Patient preparation and precautions

1. Prearrival and patient instructions

Patients may require a careful explanation of the procedure and constant reminders of the need for cooperation. It is often helpful to have a family member or guardian present to help with reassurance and to explain the procedure in a manner that is understood by the patient.

Patients who are unable to cooperate with the examination may need sedation. The sedation method will vary by patient and may need to be determined on the basis of the information provided by the referring physician. Sedation should be arranged at the time an amyloid PET examination is scheduled so that the procedure will go smoothly and without delay.

It is not known whether amyloid PET radiotracers have harmful fetal effects. Although pregnancy is often not relevant in a dementia population, amyloid PET should be performed on a pregnant woman only if there is a clear clinical benefit. Per standard practice, pregnancy status should be confirmed before administering a radiotracer to a female patient of reproductive potential.

Similarly, breastfeeding is rarely a concern for dementia patients. It is not known if amyloid PET tracers have harmful effects on infants or breast tissue. However, for caution in this rare instance and because of the potential for radiotracer excretion in human milk and potential radiation exposure to infants, either avoid performing amyloid PET imaging on a breastfeeding mother or have the mother interrupt breastfeeding for 24 h after administration of the 18F radiotracer.

There is no known evidence to suggest that there are drug interactions between amyloid radiotracers and common drugs prescribed for dementia patients, such as donepezil, galantamine, and memantine. No drug withdrawal is recommended at this time.

2. Information pertinent to the procedure

Several parameters should be taken into consideration in order to improve the quality of the study acquisition and reporting.

Correlation (preferably using digital image coregistration) with recent or concurrent morphologic imaging studies (e.g., CT or MRI) is recommended to evaluate the amount and location of brain atrophy as well as other anatomic changes such as encephalomalacia from prior stroke, brain surgery, or head trauma, which may affect amyloid PET scan interpretation.

Correlation of amyloid PET results with prior PET or SPECT brain studies may be performed, although interpretation of the amyloid PET scan should be done independently of clinical or other imaging data (other than the morphologic imaging just mentioned).

The patient’s ability to lie still for the duration of the acquisition should be assessed before injection of the radiotracer.

For patients requiring sedation, 18F-labeled radiopharmaceuticals should be injected before the administration of sedation to minimize any theoretic effects of sedatives on cerebral blood flow and radiotracer delivery.

3. Precautions

General precautions are recommended on handling the 18F-labeled radiopharmaceutical solution, such as the precaution of using aseptic technique during the injection and appropriate radiation shielding. The dose must be assayed in a suitable calibrator before administration. The injection site should be routinely inspected for dose infiltration.

Specific precautions should be taken for an amyloid PET examination. The radiopharmaceutical dose solution should be inspected before administration. It should not be used if it contains particulate matter or is discolored. The radiotracer should be injected using a short intravenous catheter (4 cm [1.5 inches] or less) to minimize the potential for adsorption of substantial amounts of the drug to the catheter. Portions of the radiotracer dose may readily adhere to longer catheters.

C. Radiopharmaceuticals

Several radiotracers for amyloid PET have been investigated. A wealth of information is available on the radiotracer 11C-Pittsburgh compound B, followed by growing numbers of publications on the 18F-labeled compounds. As of 2014, 18F-florbetapir (Amyvid), 18F-flutemetamol (Vizamyl), and 18F-florbetaben (NeuraCeq) have been approved by both the U.S. and the European authorities. Although these radiotracers share a common imaging target and similar imaging characteristics, Aβ tracers can differ in their tracer kinetics, specific binding ratios, and optimal imaging parameters (11) and hence will have different recommended injected doses, times to initiate imaging after injection, and scan durations.

D. Image acquisition

Before scanning, patients should empty their bladder for maximum comfort during the study. They should be supine and have a suitable head support. To reduce the potential for head movement, patients should be as comfortable as possible, with the head secured completely. Tape or other flexible head restraints may be required for tracer delivery.

The imaging protocol for 18F-florbetapir, 18F-flutemetamol, and 18F-florbetaben are described here. The radiotracer should be injected as a single intravenous slow bolus in a total volume of 10 mL or less. The catheter should be flushed with at least 5–15 mL of 0.9% sterile sodium chloride to ensure full delivery of the dose. The recommended dose, waiting period, and acquisition duration are summarized in Table 1. Images should be acquired in 3-dimensional mode with appropriate data corrections and reconstructed using attenuation correction with typical transaxial pixel sizes of 2–3 mm and a slice thickness of 2–4 mm.

The patient should be advised to hydrate and void after the scanning session to diminish radiation exposure.

Acquisition of early postinjection images reflecting cerebral blood flow has been described as an aid for better image interpretation and improved accuracy for 18F-florbetapir (12). Such methods and their diagnostic values are currently under investigation.
E. Interpretation

The specific criteria for amyloid PET image interpretation may differ among available radiotracers, and interpreters should be aware of the Food and Drug Administration or European Medicines Agency recommendations specific to a given amyloid tracer. The following general principles should be applied to the interpretation of amyloid PET scans.

PET images should have at least 16-bit pixels to provide an adequate range of values, and appropriate image scaling should be used for display. Gray scale display is preferred, but a specific color scale may be used, as recommended by the manufacturer for \(^{18}F\)-flutemetamol. For \(^{18}F\)-florbetaben and \(^{18}F\)-florbetapir, PET images should be displayed in the transaxial orientation using gray scale or inverse gray scale. Correlated display of coronal and sagittal planes may be used to help define the tracer uptake and to ensure that the entire brain has been reviewed.

Image size should be optimized in order to evaluate gray–white matter differentiation. For \(^{18}F\)-florbetapir, the maximum intensity of the display scale should be set to the brightest region of overall brain uptake. For \(^{18}F\)-florbetaben, the manufacturer recommends using the white matter maximum as the reference. For \(^{18}F\)-flutemetamol, the manufacturer recommends setting the scale intensity in the pons region to 90%.

Review of transaxial images from the bottom to the top of the brain allows for initial confirmation of normal gray–white matter differentiation in the cerebellum. The cerebellar cortex is expected to be generally free of A\(\beta\) deposition even in subjects with cerebral cortical amyloid disease. Thus, the cerebellar gray matter and white matter should always be clearly delineated from each other. All cerebral cortical and subcortical regions should then be screened for gray matter radiotracer uptake. Specific attention should be paid to the lateral temporal, frontal, posterior cingulate/precuneus, and parietal cortices, but also the basal ganglia. The gray matter intensity of the cerebellar cortex is usually less than that of cerebral cortical regions on a normal scan because of closer proximity of white matter structures in the latter. If image quality is significantly degraded by head motion, rescanning or rescheduling should be considered.

Negative amyloid PET scans normally show nonspecific white matter uptake and little or no binding in the gray matter. Thus, negative scans have a clear gray–white matter contrast. The amount of normal white matter uptake varies with the radiotracer used. The uptake pattern in A\(\beta\)-negative subjects resembles a blueprint of white matter distribution (white matter sulcal pattern) with numerous concave arboreal ramifications not reaching into the cortical ribbon. A clear, wide, irregular gap between the cerebral hemispheres will usually be visible.

Regarding positive scans, in patients with significant amounts of A\(\beta\) deposition in the brain, radiotracer uptake in gray matter blurs the distinction of the gray–white junction. Thus, a key feature for distinguishing A\(\beta\)-positive from -negative patients is loss of gray–white matter contrast, with radiotracer uptake extending to the edge of the cerebral cortex and forming a smooth, regular boundary. Radiotracer uptake may drop sharply at the cortical margin, and a convex outer surface of the brain may be outlined rather than the white matter sulcal pattern typical of a negative scan. Gaps between the two hemispheres may no longer be defined or, if seen, may appear as a thin, regular line. Abnormal radiotracer uptake tends to be symmetric, affecting both right and left lobar structures. Cortical regions exhibiting the most distinct radiotracer accumulation in A\(\beta\)-positive subjects typically include the lateral temporal and frontal lobes, as well as the posterior cingulate cortex/precuneus and the parietal lobes, whereas the sensorimotor cortex and the visual cortex can be relatively spared. Striatal radiotracer uptake, most notable in the caudate head, is also often found and may be decisive in subjects with major cortical atrophy. In patients with hereditary forms of AD, uptake that is particularly intense in the striatum has been described (\(f\)). The cerebellar cortex does not usually show radiotracer uptake in most amyloid-positive subjects. Thus, the cerebellum can generally be used as a reference region for visual and semiquantitative interpretation. The radiotracer package inserts provide specific guidelines on the number of affected cortical regions required for definition of a positive scan. An intermediate (or indeterminate) scan pattern may also be encountered.

Some scans may be difficult to interpret because of image noise, atrophy with a thinned cortical ribbon, or image blurring. Atrophied brain may lead to false-positive results due to overestimation of radiotracer uptake in the remaining cortex based on spillover from the white matter uptake. Atrophied brain may lead to false-negative results in cases of severe atrophy, rendering it impossible to differentiate a thin ribbon of amyloid-positive cortex from adjacent white matter. The latter cases may erroneously resemble the typical appearance of nonspecific white matter uptake in a healthy control subject. When there is uncertainty as to the location or edge of gray matter on the PET scan and a coregistered CT image is available (as when the scan is done on a PET/CT scanner), the interpreter should examine the CT or fused images to clarify the tissue to which radiotracer uptake localizes. If a current MRI study is available, coregistration of PET and MRI data can also provide useful information, especially on localization of cortical (gray–white matter) radiotracer uptake. The clinical introduction of hybrid PET/MRI scanners may help to further improve visual and quantitative data analysis as well as scanning procedures and diagnostic discrimination.

<table>
<thead>
<tr>
<th>Radiotracer</th>
<th>Dose</th>
<th>Wait (min)</th>
<th>Acquisition (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^{18}F)-florbetapir</td>
<td>370 MBq (10 mCi)</td>
<td>30–50</td>
<td>10</td>
</tr>
<tr>
<td>(^{18}F)-flutemetamol</td>
<td>185 MBq (5 mCi)</td>
<td>90</td>
<td>20</td>
</tr>
<tr>
<td>(^{18}F)-florbetaben</td>
<td>300 MBq (8 mCi)</td>
<td>45–130</td>
<td>20</td>
</tr>
</tbody>
</table>

Variability in recommended dose is based on differences in absorbed radiation dose (Table 2).
If a perfusion SPECT or 18F-FDG PET scan is available, correlation with areas of decreased function may assist in such uncertain cases.

Amyloid PET results should be interpreted independently of clinical information, but the final report may integrate scan findings and clinical information and suggest a final or differential diagnosis and patient management plan. Commenting on any correlation with other available imaging data may be helpful to the referring physician.

Visual interpretation comprises a qualitative binary interpretation algorithm of a positive or negative scan. Semi-quantitative techniques may be helpful, including use of parametric SUV ratio images. These and other methods and their diagnostic values are currently under investigation. Absolute quantitative measurements of amyloid tracer binding in the brain using a dynamic PET imaging protocol and tracer kinetic analysis are not required clinically but may be used for research purposes.

For radiotracers that have not been approved by the Food and Drug Administration or the European Medicines Agency (e.g., 11C-Pittsburgh compound B), and in certain countries, imaging principles similar to those in this standard/guideline may apply.

### VI. DOCUMENTATION/REPORTING

General recommendations on nuclear medicine reports are provided in the SNMMI Procedure Standard on General Nuclear Imaging and the ACR Practice Guideline for Communication: Diagnostic Radiology.

#### A. Indications

The specific clinical symptoms of MCI or dementia should be documented, and the reasons for the test (e.g., uncertain clinical diagnoses, atypical age of onset, known comorbidities, or for clinical trial) should be briefly described. A management plan based on the test findings may be briefly described.

#### B. Technique

The name of the radiotracer used and the dose of radioactivity administered should be clearly documented, as well as the time between injection of radiotracer and scanning. Any difficulty with radiotracer injection (particularly infiltration) should also be documented. The imaging technology used (PET, PET/CT, or PET/MRI) should be noted, along with the methods of data acquisition, reconstruction, and attenuation correction.

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**TABLE 2**

Estimated Mean Absorbed Radiation Doses per Unit of Administered Activity

<table>
<thead>
<tr>
<th>Organ or tissue</th>
<th>18F-florbetapir</th>
<th>18F-flutemetamol</th>
<th>18F-florbetaben</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal</td>
<td>14</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Brain</td>
<td>10</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Breasts</td>
<td>6</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Gallbladder wall</td>
<td>143</td>
<td>287</td>
<td>137</td>
</tr>
<tr>
<td>Heart wall</td>
<td>13</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Kidneys</td>
<td>14</td>
<td>40</td>
<td>24</td>
</tr>
<tr>
<td>Liver</td>
<td>64</td>
<td>64</td>
<td>39</td>
</tr>
<tr>
<td>Lower large intestine wall</td>
<td>28</td>
<td>81</td>
<td>35</td>
</tr>
<tr>
<td>Lungs</td>
<td>9</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Muscle</td>
<td>9</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Osteogenic cells</td>
<td>28</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Ovaries</td>
<td>18</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>Pancreas</td>
<td>14</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Red marrow</td>
<td>14</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Skin</td>
<td>6</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Small intestine</td>
<td>66</td>
<td>155</td>
<td>31</td>
</tr>
<tr>
<td>Spleen</td>
<td>9</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>Stomach wall</td>
<td>12</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Testes</td>
<td>7</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Thymus</td>
<td>7</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Thyroid</td>
<td>7</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Upper large intestine wall</td>
<td>74</td>
<td>173</td>
<td>38</td>
</tr>
<tr>
<td>Urinary bladder wall</td>
<td>27</td>
<td>62</td>
<td>70</td>
</tr>
<tr>
<td>Uterus</td>
<td>16</td>
<td>27</td>
<td>16</td>
</tr>
<tr>
<td>Total body</td>
<td>12</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Effective dose (μSv/MBq)</td>
<td>19</td>
<td>34</td>
<td>19</td>
</tr>
</tbody>
</table>
C. Findings

The pattern of radiotracer uptake in the cerebellum should be discussed, and the degree and location of cerebral atrophy (if present) should be described. If there is a loss of gray–white matter differentiation, the affected lobes should be noted. Any areas in which cerebral cortical uptake is more intense than white matter uptake should be noted.

D. Impression

Amyloid PET scanning depicts Aβ deposition in the brain, but it is critically important to note that a scan positive for Aβ deposition is not in itself indicative of AD. Positive findings can occur in non-AD forms of dementia (e.g., dementia with Lewy bodies) and other neurologic diseases and can also occur in older subjects without cognitive impairment. Also, a positive amyloid PET result does not exclude other coexistent disorders (e.g., AD plus progressive supranuclear palsy). Negative results indicate patients who are unlikely to have AD at the time of imaging. Negative results among MCI patients also indicate that they are unlikely to advance to AD dementia. However, negative results do not exclude the presence of a non-AD dementing illness.

The impression should state clearly whether the scan demonstrates moderate or frequent Aβ deposition in the cerebral cortex (positive result) or no evidence of significant Aβ deposition (negative result). An alternative would be stating that the scan demonstrates or does not demonstrate significant Aβ deposition. Also, an acceptable statement may be that the findings are consistent with the presence or absence of significant Aβ deposition. If the scan is indeterminate and inconclusive, this needs to be stated along with possible reasons, such as low counting rate, head motion during imaging, unexpected focal lesion, cortical atrophy, or other difficulties. The impression should not include statements such as “the scan is diagnostic of Alzheimer disease.”

VII. EQUIPMENT SPECIFICATION

Amyloid PET scans may be acquired on PET, PET/CT, or PET/MR systems from various manufacturers. The newest-generation scanners typically offer the best image resolution and differentiation of gray matter from white matter. Adequate knowledge of the technique and equipment used is required for good quality and to avoid artifacts. For Aβ brain scans, a dedicated head holder is important for positioning the head and limiting its motion. If a PET/CT or PET/MR system is not used, attenuation correction must be used. All PET scanners need to undergo periodic quality control tests per manufacturer specifications and pass certification requirements. The SNMMI Procedure Standard on General Imaging provides more specific recommendations.

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

The SNMMI Procedure Standard on General Imaging provides general recommendations.

Standard quality controls for every system have to be maintained per manufacturer specifications. Locally developed policies and procedures related to quality, patient education, infection control, and safety should be followed. Visual inspection is mandatory to ensure the quality of the radiotracer, which should not have any precipitation or haziness. Dose calibrator quality control should be performed at regular intervals. A dose assay of the syringe should always be performed before and after injection. The injection site should be imaged to ensure absence of dose infiltration either systematically or when a study appears noisy or shows an unexpectedly poor counting rate. This imaging option can be determined by individual sites.

Quality control standards need to be assessed to avoid misinterpretations resulting from poor image quality due to a low-count study (from poor labeling or dose infiltration), brain atrophy, bone marrow uptake in the skull, head motion, or poor head positioning.

Patient safety can be of particular concern for patients with dementia, who are often unsteady or osteoporotic or can injure themselves because of cognitive difficulties. Patients should be assisted carefully when walking in the imaging department and when getting on and off the imaging equipment. Obstacles in the room should be minimized. Sharp, unstable, or otherwise dangerous objects should be kept out of the reach of patients. When patients are being restrained on the bed or in a head holder, they should be provided with frequent explanations and reassurance to help prevent fear or resistance.

Imaging of the head is optimal when the cerebrum and cerebellum are fully in the center of the axial field of view.

Sedation may be given after radiotracer injection if needed to minimize head motion, but—if the patient has cognitive impairment or dementia—only after careful medical evaluation. Sedated patients will need closer monitoring during and after the study until the effects have worn off. Sometimes paradoxical activation occurs in elderly patients. However, sedation should be avoided in elderly patients as much as possible.

Patients may have difficulty understanding the reason for the procedure. A family member or guardian can sometimes assist communication and compliance with instructions during the examination.

The risk of adverse events caused by the radiotracer is typically low, at less than 2%, and may include headaches, nausea, dizziness, flushing, increased blood pressure, musculoskeletal pain, or an injection site reaction. The individual package inserts provide full side effect profiles.

IX. RADIATION SAFETY IN IMAGING

It is the position of SNMMI that exposure of patients to ionizing radiation should be at the minimum level consistent with obtaining a diagnostic examination (see the SNMMI Procedure Standard on General Imaging). Currently approved amyloid PET tracers offer a reasonable compromise between radiation exposure following ALARA (as low as reasonably achievable) principles and image quality. The radiation exposure from an amyloid PET study—at about 4–7 mSv—is within the range of commonly performed imaging studies. Radiation dosimetry estimates in humans have been evaluated in pilot studies for 18F-florbetapir and 18F-flutemetamol (13,14), as well as in the 18F-florbetapir (15) and 18F-flutemetamol clinical trials. Florbetaben dosimetry has been previously published (16).

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XI. REFERENCES


XII. APPROVAL

This standard/guideline was approved by the Board of Directors of the SNMMI on January 30, 2016, and by the EANM Board on February 10, 2016.
SNMMI Procedure Standard/EANM Practice Guideline for Amyloid PET Imaging of the Brain 1.0

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