**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. The European Association of Nuclear Medicine (EANM) is a professional non-profit medical association that facilitates communication worldwide between individuals pursuing clinical and research excellence in nuclear medicine. The EANM was founded in 1985. SNMMI and EANM members are physicians, technologists, and scientists specializing in the research and practice of nuclear medicine. The SNMMI and EANM will periodically define new guidelines for nuclear medicine practice to help advance the science of nuclear medicine and to improve the quality of service to patients throughout the world. Existing practice guidelines will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.**

 **Each practice 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 and EANM recognize that the safe and effective use of diagnostic nuclear medicine imaging requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice guideline by those entities not providing these services is not authorized.**

**SNMMI-EANM Standard for Amyloid PET Imaging of the Brain**

**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 17,000 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 standard/guidelines will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated. As of February 2014, the SNMMI guidelines will now be referred to as procedure standards. Any previous practice guideline or procedure guideline that describes how to perform a procedure 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. GOALS/OBJECTIVES**

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

**II. INTRODUCTION/DEFINITIONS**

Extracellular deposition of amyloid β (Aβ) peptides (or “plaques”) is one of the pathological hallmarks of Alzheimer’s disease [1](#_ENREF_1). The recent developments of molecular imaging tracers that bind to Aβ plaques in the brain have enabled in vivo detection of Aβ plaque deposition using positron emission tomography (PET). Non-invasive detection of Aβ deposition may 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 2014, three compounds have been approved for imaging Aβ plaques by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA): 18F-Florbetapir (Amyvid**™**, Eli Lilly); 18F-Flutemetamol (Vizamyl**™**, GE Healthcare); and 18F-Florbetaben (NeuraCeqTM, 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 neuropathological 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’s Association (NIA-AA) and the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) published updated consensus guidelines for the *neuropathological* assessment of Alzheimer’s disease [2](#_ENREF_2), [3](#_ENREF_3). This guideline defines AD as a clinicopathological entity, instead of neuropathological disease confirmed at autopsy, with a set of clinical signs and symptoms of cognitive and behavioral changes that are typical for patients who have substantial AD neuropathological changes. The NIA-AA consensus guideline describes 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.

**Pre-AD or pre-clinical AD** is defined as the prodromal phase where a series of pathologic events are occurring in the brain including Aβ buildup prior to the onset of significant and clinically detectable symptoms.

**Mild cognitive impairment (MCI)** is marked by clinical symptoms of memory and/or other cognitive problems greater than normal for age and education. These symptoms are mild enough that they do not 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 and not everyone with MCI may have AD, and MCI patients may or may not progress to dementia. However, the risk of conversion to clinically manifest dementia is significantly increased in MCI and, thus, MCI can be considered as a risk factor to developing AD dementia. Other entities that may benefit from amyloid imaging biomarker includes the groups of “Probable AD” dementia [4](#_ENREF_4) [5](#_ENREF_5) and “Possible AD” dementia [6](#_ENREF_6).

**III. COMMON CLINICAL INDICATIONS**

Appropriate use criteria (AUC) for amyloid PET have been published recently by the SNMMI and AA joint taskforce [7-9](#_ENREF_7). The AUC emphasize that amyloid PET is currently most likely to be helpful when the patient has:

1. Objectively confirmed cognitive impairment and
2. The cause of cognitive impairment remains uncertain after a comprehensive evaluation by a dementia expert and the differential diagnosis includes AD dementia and
3. Knowledge of the presence or absence of Aβ pathology is expected to increase diagnostic certainty and/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 Alzheimer’s disease [7](#_ENREF_7).

The use of amyloid PET is considered appropriate in patients with any of the following conditions:

1. Persistent or progressive unexplained MCI.
2. 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-.
3. Patients with progressive dementia and atypically early age of onset (usually defined as 65 years or less in age).

The use of amyloid PET is considered inappropriate for:

1. Patients with core clinical criteria for probable AD with typical age of onset
2. Determination of dementia severity
3. Asymptomatic individuals with a positive family history of AD or have been shown to carry the ε4 allele of apolipoprotein E (APOE-ε4 genotype).
4. Patients with a cognitive complaint that is unconfirmed on clinical examination
5. In lieu of genotyping for suspected autosomal dominant mutation carriers
6. Asymptomatic individuals
7. Nonmedical use (e.g., legal, insurance coverage, or employment screening)

Please note that the above AUC 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**

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

Technologist: Amyloid PET examinations should be performed by qualified registered/certified Nuclear Medicine Technologists. Please refer to: Performance Responsibility and Guidelines for Nuclear Medicine Technologists 3.1 for further details.

**V. PROCEDURE/SPECIFICATIONS OF THE EXAMINATION**

### *See also the SNM Guideline for General Imaging.*

As of the end of 2014, 18F-Florbetapir, 18F-Flutemetamol and 18F-Florbetaben have been approved by the FDA and EMA in the USA and Europe, respectively, for amyloid PET examinations. Although these tracers share a common imaging target and similar imaging characteristics, amyloid tracers can differ in their tracer kinetics, specific binding ratios, and optimal imaging parameters [10](#_ENREF_10).

### Nuclear Medicine Study Request:

The nuclear medicine department should check with their local nuclear pharmacy provider as to the availability of the radiotracer before scheduling the exam. Advanced notice may be required for tracer delivery.

The study requisition should include 1) appropriate clinical information about the patient to justify the study and to allow appropriate exam/study coding ; 2) information about the ability of the patient to cooperate for the test is helpful; and 3) 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. Pre-arrival and Patient Instructions:

## Patients may require careful explanation of the procedure and constant reminders of the need for their 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.

1. Patients who are unable to cooperate for the examination may need sedation. The sedation method will vary by patient and may need to be determined based on the information provided by the referring physician. Sedation should be arranged at the time of scheduling an amyloid PET examination so that the procedure will go smoothly without delay (See 2-d below).
2. It is not known if amyloid PET radiotracers have harmful fetal effects. Although pregnancy is often not relevant in a dementia population, amyloid PET should be performed in a pregnant woman only if there is a clear clinical benefit. Pregnancy status should be confirmed before administering a radiotracer to a female of reproductive potential.
3. 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, because of the potential for radiotracer excretion in human milk and potential radiation exposure to infants, avoid performing amyloid PET imaging in a breastfeeding mother or have the mother temporarily interrupt breastfeeding for 24 hours after administration of the 18F radiotracer decay.

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:

1. Correlation (preferably using digital image coregistration) with recent or concurrent morphologic imaging studies (e.g. CT, MRI) is recommended to evaluate the amount and location of brain atrophy as well as other anatomical changes such as encephalomalacia from prior stroke, surgery or trauma, which may affect amyloid PET scan interpretation.
2. 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 “a” above).
3. The patient’s ability to lie still for the duration of the acquisition should be assessed prior to injection of the radiotracer.
4. For patients requiring sedation, 18F-labeled radiopharmaceuticals should be injected prior to the administration of sedation in order to minimize any theoretical effects of sedatives on cerebral blood flow and radiotracer delivery.

3. Precautions

1. General precautions are recommended in regards to using aseptic techniques during the injection and appropriate radiation shielding when handling the 18F-labeled radiopharmaceutical solution. Assaying the dose must be performed in a suitable dose calibrator prior to administration. Inspection of the injection site should be carried out for any dose infiltration.
2. Specific precautions should be taken with an amyloid PET examination: Inspect the radiopharmaceutical dose solution prior to administration. It should not be used if it contains particulate matter or is discolored. The tracer should be injected using a short intravenous catheter (approximately 1.5 inches -4 cm- 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 (PIB), followed by growing numbers of publications on the 18F-labeled compounds. As of 2014, 18F-Florbetapir (Amyvid**™**,Eli Lilly); 18F-Flutemetamol (Vizamyl**™**, GE Healthcare); and 18F-Florbetaben (NeuraCeqTM, Piramal Pharma) have been approved by both US and European authorities. Although these tracers share a common imaging target and similar imaging characteristics, Aβ tracers can differ in their tracer kinetics, specific binding ratios, and optimal imaging parameters [10](#_ENREF_10) and hence will have different recommended injected doses, time to initiate imaging post injection, and scan duration.

D. Protocol/Image acquisition

Imaging protocols for 18F-Florbetapir, 18F-Flutemetamol, and 18F-Florbetaben are described here.

1. Before scanning, the patient should empty their bladder for maximum comfort during the study.
2. The patient should be supine with suitable head support. The entire brain should be in the field of view, including the entire cerebellum. Avoid extreme neck extension or flexion if possible. To reduce the potential for head movement, the patient should be as comfortable as possible with the head secured as completely as possible. Tape or other flexible head restraints may be employed and are often helpful.
3. Dose/Radiotracer quality control should be followed as outlined in section VI.B.3b. 18F-Florbetapir, 18F-Flutemetamol and 18F-Florbetaben should be injected as a single intravenous slow-bolus in a total volume of 10 ml or less. The dose/catheter should be flushed with at least 5-15 ml 0.9% sterile sodium chloride to ensure full delivery of the dose.
4. The recommended dose/activity, waiting period, and image acquisition duration are summarized in the following table:

|  |  |  |  |
| --- | --- | --- | --- |
| **Radiotracer** | **Recommended Dose/Activity** | **Waiting Period** | **Acquisition** |
| 18F-Florbetapir | 370 MBq (10 mCi) | 30-50 minutes | 10 minutes |
| 18F-Flutemetamol | 185 MBq (5 mCi) | 90 minutes | 20 minutes |
| 18F-Florbetaben | 300 MBq (8 mCi) | 45-130 minutes | 20 minutes |

 Note should be made that variability in recommended activities administered are based on differences in radiation exposure rates. Please see radiation dosimetry table in section X.

1. Image acquisition should be performed in 3D data acquisition mode with appropriate data corrections.
2. Image reconstruction should include attenuation correction with typical transaxial pixel sizes between 2-3 mm and slice thickness between 2-4 mm.
3. Advise the patient to hydrate and void after the scanning session to diminish radiation exposure.

Note that optional acquisition of early flow images has been described as an aid for better image interpretation and improved accuracy[11](#_ENREF_11).

E. Interpretation

The specific criteria for amyloid PET image interpretation may differ among available tracers, and readers should be aware of the FDA or EMA recommendations specific to a given amyloid tracer. The following general principles should be applied to the interpretation of amyloid PET scans:

1. Image display: PET images should have at least 16-bit pixels to provide an adequate range of values, and appropriate image scaling should be employed for image display. Gray scale display is preferred, but a specific color scale may be used –as recommended by the manufacturer for 18F-Flutemetamol-. For 18F-Florbetaben, and 18F-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.
2. Image size should be optimized in order to evaluate gray-white matter differentiation. The maximum intensity of the display scale should be set to the brightest region of overall brain uptake for 18F-Florbetapir. The white matter maximum has been suggested as a reference for 18F-Florbetaben by the manufacturer. For 18F-Flutemetamol it is recommended by the manufacterer to set the scale intensity to a level of 90% in the pons region.
3. Review of transverse 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 from Aβ deposition even in subjects with cortical amyloid pathology. Thus, clear gray/white matter delineation in the cerebellum should always be visible. All cerebral cortical regions and subcortical regions should then be screened for gray matter tracer uptake. Specific attention should be paid to the lateral temporal, frontal, posterior cingulate/precuneus, and parietal cortices, but also the basal ganglia (see below). Note that the gray matter intensity of the cerebellar cortex is usually less than the gray matter intensity in cortical regions in a normal scan owing to closer proximity of white matter structures in the latter.
4. Negative scan: Negative amyloid PET scans normally show non-specific 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 tracer used. The uptake pattern in Aβ -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 gap between the cerebral hemispheres will usually be visible, wide and irregular.
5. Positive scan: In patients with significant amounts of Aβ deposition in the brain, tracer uptake in gray matter blurs the distinction of the gray/white junction. Thus, a key feature for distinguishing Aβ 'positive' from 'negative' patients is loss of gray/white matter contrast, with tracer uptake extending to the edge of the cerebral cortex forming a smooth, regular boundary. Tracer 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 for a negative scan. Gaps between the two hemispheres may no longer be defined or if seen, appear as a thin regular line. Abnormal radiotracer uptake tends to be symmetrical, affecting both right and left lobar structures. Cortical regions exhibiting the most distinct tracer accumulation in Aβ -positive subjects typically include lateral temporal and frontal lobes as well as posterior cingulate cortex/precuneus, and the parietal lobes, whereas the sensorimotor cortex and the visual cortex can be relatively spared. Striatal tracer 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 particularly intense uptake in the striatum has been described [1](#_ENREF_1). The cerebellar cortex does not usually show tracer uptake in the majority of amyloid-positive subjects. Thus, the cerebellum can generally be used as a reference region for visual as well as for semi-quantitative interpretation. For specific guidelines on the number of affected cortical regions required for definition of a “positive” scan, refer to the tracer package inserts. An intermediate (or indeterminate) scan pattern may also be encountered.
6. Some scans may be difficult to interpret due to image noise, atrophy with a thinned cortical ribbon, or image blur. Atrophied brain may lead to false positives due to overestimation of tracer uptake in remaining cortex based on spillover from the white matter uptake and to false negatives in cases with 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 non-specific white matter uptake in a healthy control. For cases in which there is uncertainty as to the location or edge of gray matter on the PET scan and a co-registered computerized tomography (CT) image is available (as when the study is done on a PET/CT scanner) the interpreter should examine the CT and or fused images and clarify to which tissue the tracer uptake localizes. If a current MRI is available, a co-registration of PET and MRI data could also provide useful information especially in localization of cortical (gray/white matter) tracer uptake. The clinical introduction of hybrid PET/MRI scanner may help to further improve visual and quantitative data analysis as well as scanning procedures and diagnostic work-up. If a perfusion SPECT or a FDG PET scan is available, then correlation with areas of decreased function may assist in such uncertain cases.
7. Amyloid PET scan interpretation should be done independent of clinical information, but the final reporting may integrate scan findings and clinical information and suggest appropriate diagnosis and differential diagnosis and management of the patient as appropriate. Commenting on correlation with other available imaging data may be helpful to the referring physician.
8. Visual interpretation comprises a qualitative binary reading algorithm of a positive or negative scan. Semi-quantitative techniques may be helpful, including use of parametric SUVR images and the 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.

**NOTE: For non-FDA/EMEA approved tracers (such as 11C-PIB), and in certain countries; similar imaging principles as in this guideline may apply as appropriate.**

**VI. DOCUMENTATION/REPORTING**

*For general recommendations for all Nuclear Medicine reports see the SNMMI Guideline on General Nuclear Imaging and ACR Practice Guideline for Communication: Diagnostic Radiology.*

1. Indications
	1. The specific clinical symptoms of mild cognitive impairment or dementia should be documented.
	2. Reasons for the test (i.e., 'uncertain clinical diagnosis', 'atypical onset of age', 'known comorbidities', 'for clinical trial') should be briefly described.
	3. A management plan based on the test findings may be briefly described.
2. Technique
	1. The name of the tracer used and dose of radioactivity administered should be clearly documented.
	2. The length of time between injection of tracer and scanning should be documented.
	3. Any difficulty with tracer injection (particularly infiltration) should be documented.
	4. Imaging technology (PET or PET/CT or PET/MRI) should be documented along with the methods of data acquisition, reconstruction, and attenuation correction.
3. Findings
	1. The pattern of tracer uptake in the cerebellum should be discussed.
	2. The degree and location of cerebral atrophy (if present) should be described.
	3. If present, the lobes where the loss of gray/white matter differentiation is noted should be described.
	4. If present, any areas with cerebral cortical uptake more intense than white matter uptake should be described as such, along with location.
4. Impression
5. Amyloid PET scan depicts Aβ deposition in the brain, but it is critically important to note that a 'positive' scan is not by itself indicative of AD. Positive scans can occur in non-AD forms of dementia (such as Dementia with Lewy bodies) as well as other neurological diseases and can also occur in older subjects without cognitive impairment. Also, a positive amyloid PET does not exclude concomitant disorders (such as AD + progressive supranuclear palsy). Negative scans indicate patients who are unlikely to be suffering from AD at the time of imaging. Negative scans among MCI patients also indicate that they are unlikely to advance to AD dementia. However, negative scans do not exclude the presence of a non-AD dementing illness.
6. The impression should state clearly if the scan demonstrates “moderate or frequent” Aβ deposition in the cerebral cortex ('positive' scan) or “no evidence of significant Aβ deposition” ('negative' scan). An alternative would be stating that this 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 count 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’s disease”.

**VII. EQUIPMENT SPECIFICATION**

Amyloid PET scans may be acquired on PET, PET/CT and PET/MR systems from various manufacturers. The newest generation scanners typically offer the best image resolution and differentiation of gray/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 very important in positioning the head appropriately and limiting patient head motion. If a PET/CT or PET/MR system is not used, attenuation correction using an attenuation source or calculated attenuation correction must be employed. All PET scanners need to undergo regular quality control per manufacturer specifications and pass certification requirements. Please see the SNMMI General Imaging Guideline for more specific recommendations.

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

Please also see the SNMMI General Imaging Guideline for general recommendations.

1. 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 of the tracer is mandatory to ensure the quality of the tracer, which should NOT have any precipitation or haziness. Dose calibrator QC should be performed regularly. The dose assay of the syringe should always be performed pre and post-injection. The injection site should be imaged to ensure absence of dose infiltration either systematically or when a study appears noisy/shows an unexpectedly poor count rate. This imaging option can be determined by individual sites.
2. Quality control standards need to be assessed to avoid misinterpretations resulting from poor image quality due to a low count study (from poor labeling, dose infiltration), brain atrophy, bone marrow uptake in the skull, head motion, and head positioning.
3. Patient safety can be of particular concern in patients with dementia who are often unsteady, osteoporotic, or can injure themselves because of cognitive difficulties.
	1. Patients should be assisted carefully when ambulating in the imaging department and when getting on and off the imaging equipment.
	2. Obstacles in the room should be minimized.
	3. Sharp, unstable or otherwise dangerous objects should be kept out of reach of the patient.
	4. When restraining patients on the bed or in a head holder, frequent explanation and reassurance should be used to help the patient from becoming frightened or resistant.
4. Imaging of the head is optimal when the head is in the center of the field of view. The cerebrum and cerebellum should be fully in the axial FOV.
5. Sedation may be needed to minimize head motion. Sedation may be given after radiotracer injection. Sedation in patients with cognitive impairment or dementia should be performed only after careful medical evaluation. Sedated patients will need closer monitoring during and after the study until the sedative effects have worn off. Sometimes paradoxical activation occurs in elderly patients. However, sedation should be avoided in elderly patients as much as possible.
6. Patients may have difficulty understanding the reason for the examination and the procedure. A family member or guardian can sometimes assist communication and compliance with the instructions during the examination.
7. The risk of adverse events caused by the radiotracer is low on average < 2% and may include headaches, nausea, dizziness, flushing, increased blood pressure, musculoskeletal pain, injection site reaction. Please see individual package inserts for full side effect profile.

**IX. RADIATION SAFETY IN IMAGING**

It is the position of SNMMI that patient exposure to ionizing radiation should be at the minimum level consistent with obtaining a diagnostic examination (*See the SNMMI Guideline for General Imaging).* Currently approved amyloid PET tracers offer a reasonable compromise between radiation exposure following ALARA principles and image quality. The radiation exposure from an amyloid PET study is well within clinically approved imaging doses. It is estimated to be in the range of about 4-7 mSv. Radiation dosimetry estimates in humans have been evaluated in pilot studies for 18F- Florbetapir and 18F-Flutemetamol respectively [12](#_ENREF_12) [13](#_ENREF_13) as well as the 18F- Florbetapir [14](#_ENREF_14) and 18F-Flutemetamol clinical trials. Please refer to O'Keefe et al for Florbetaben dosimetry [15](#_ENREF_15) .

**Estimated Radiation Absorbed Dose, Amyvid (Florbetapir F 18 Injection), Vizamyl (Flutemetamol F 18 injection) and Neuraceq (Florbetaben F 18 Injection)**

|  |  |  |  |
| --- | --- | --- | --- |
| **ORGAN/TISSUE** | **MEAN ABSORBED DOSE PER Unit ADMINISTERED ACTIVITY (µSv/MBq)** | **MEAN ABSORBED DOSE PER Unit ADMINISTERED ACTIVITY (µSv/MBq)** | **MEAN ABSORBED DOSE PER Unit ADMINISTERED ACTIVITY (µGv/MBq)** |
|  | **Florbetapir** | **Flutemetamol** | **Florbetaben** |
| Adrenal | 14 | 15 | 13 |
| Bone - Osteogenic Cells | 28 | 13 | 15 |
| Bone - Red Marrow | 14 | 15 | 12 |
| Brain | 10 | 12 | 13 |
| Breasts | 6 | 6 | 7 |
| Gallbladder Wall | 143 | 287 | 137 |
| GIa - Lower Large Intestine Wall | 28 | 81 | 35 |
| GI - Small Intestine | 66 | 155 | 31 |
| GI - Stomach Wall | 12 | 15 | 12 |
| GI - Upper Large Intestine Wall | 74 | 173 | 38 |
| Heart Wall | 13 | 12 | 14 |
| Kidneys | 14 | 40 | 24 |
| Liver | 64 | 64 | 39 |
| Lungs | 9 | 17 | 15 |
| Muscle | 9 | 10 | 10 |
| Ovaries | 18 | 33 | 16 |
| Pancreas | 14 | 17 | 14 |
| Skin | 6 | 6 | 7 |
| Spleen | 9 | 16 | 10 |
| Testes | 7 | 5 | 9 |
| Thymus | 7 | 6 | 9 |
| Thyroid | 7 | 7 | 8 |
| Urinary Bladder Wall | 27 | 62 | 70 |
| Uterus | 16 | 27 | 16 |
| Total Body | 12 | 14 | 11 |
| Effective Dose (µSv/MBq) | 19 | 34 | 19 |

**X. ACKNOWLEDGEMENTS**

*Task Force Members:*Satoshi Minoshima, MD, PhD (Co-Chair) (University of Washington, Seattle, WA); Alexander E. Drzezga, MD (Co-Chair) (University of Cologne, Cologne, Germany); Mehdi Djekidel, MD (Yale University, New Haven, CT); David H. Lewis, MD (Harborview Medical Center, Seattle, WA); Chester A. Mathis, PhD (University of Pittsburgh, Pittsburgh, PA); Jonathan McConathy, MD, PhD (Mallinckrodt, St. Louis, MO); Agneta Nordberg, MD (Karolinska Institutet, Stockholm, Sweden): Osama Sabri, MD, PhD (University Hospital Leipzig, Leipzig, Germany); John P. Seibyl, MD (Institute for Neurodegenerative Disorders, New Haven, CT); Margaret K. Stokes, CNMT (Beth Israel Deaconess Medical Center, Boston, MA); Koen Van Laere, MD, PhD (University Hospital Leuven, Leuven, Belgium); Nicolaas Bohnen, MD, PhD (University of Michigan, Ann Arbor VAMC); Henryk Barthel, MD (University Hospital Leipzig, Leipzig, Germany)

*Committee on Procedure Standards:*

Kevin J. Donohoe, MD (Chair) (Beth Israel Deaconess Medical Center, Boston, MA); Sue Abreu, MD (Sue Abreu Consulting, Nichols Hills, OK);Helena Balon, MD (Beaumont Health System, Royal Oak, MI); Twyla Bartel, DO (UAMS, Little Rock, AR); David Brandon, MD (Emory University/Atlanta VA, Atlanta, GA); Paul E. Christian, CNMT, BS, PET (Huntsman Cancer Institute, University of Utah, Salt Lake City, UT); Dominique Delbeke, MD (Vanderbilt University Medical Center, Nashville, TN); Vasken Dilsizian, MD (University of Maryland Medical Center, Baltimore, MD); James R. Galt, PhD (Emory University Hospital, Atlanta, GA); Jay A. Harolds, MD (OUHSC-Department of Radiological Science, Edmond, OK); Aaron Jessop, MD (UT MD Anderson Cancer Center, Houston, TX); David H. Lewis, MD (Harborview Medical Center, Seattle, WA); J. Anthony Parker, MD, PhD (Beth Israel Deaconess Medical Center, Boston, MA); James A. Ponto, RPh, BCNP (University of Iowa, Iowa City, IA); Lynne T. Roy, CNMT (Cedars/Sinai Medical Center, Los Angeles, CA); Heiko Schoder, MD (Memorial Sloan-Kettering Cancer Center, New York, NY); Barry L. Shulkin, MD, MBA (St. Jude Children’s Research Hospital, Memphis, TN); Michael G. Stabin, PhD (Vanderbilt University, Nashville, TN); Mark Tulchinsky, MD (Milton S. Hershey Med Center, Hershey, PA)

**XII. BIBLIOGRAPHY/REFERENCES**

**1.** Villemagne VL, Ataka S, Mizuno T, et al. High striatal amyloid beta-peptide deposition across different autosomal Alzheimer disease mutation types. *Archives of neurology.* Dec 2009;66(12):1537-1544.

**2.** Montine TJ, Phelps CH, Beach TG, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease: a practical approach. *Acta neuropathologica.* Jan 2012;123(1):1-11.

**3.** Hyman BT, Phelps CH, Beach TG, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association.* Jan 2012;8(1):1-13.

**4.** Klunk WE. Amyloid imaging as a biomarker for cerebral beta-amyloidosis and risk prediction for Alzheimer dementia. *Neurobiology of aging.* Dec 2011;32 Suppl 1:S20-36.

**5.** Dubois B, Feldman HH, Jacova C, et al. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. *Lancet neurology.* Aug 2007;6(8):734-746.

**6.** McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association.* May 2011;7(3):263-269.

**7.** Johnson KA, Minoshima S, Bohnen NI, et al. Update on appropriate use criteria for amyloid PET imaging: dementia experts, mild cognitive impairment, and education. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine.* Jul 2013;54(7):1011-1013.

**8.** Johnson KA, Minoshima S, Bohnen NI, et al. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine.* Mar 2013;54(3):476-490.

**9.** Johnson KA, Minoshima S, Bohnen NI, et al. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *Alzheimer's & dementia : the journal of the Alzheimer's Association.* Jan 2013;9(1):e-1-16.

**10.** Rowe CC, Villemagne VL. Brain amyloid imaging. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine.* Nov 2011;52(11):1733-1740.

**11.** Hsiao IT, Huang CC, Hsieh CJ, et al. Correlation of early-phase 18F-florbetapir (AV-45/Amyvid) PET images to FDG images: preliminary studies. *European journal of nuclear medicine and molecular imaging.* Apr 2012;39(4):613-620.

**12.** Lin KJ, Hsu WC, Hsiao IT, et al. Whole-body biodistribution and brain PET imaging with [18F]AV-45, a novel amyloid imaging agent--a pilot study. *Nuclear medicine and biology.* May 2010;37(4):497-508.

**13.** Koole M, Lewis DM, Buckley C, et al. Whole-body biodistribution and radiation dosimetry of 18F-GE067: a radioligand for in vivo brain amyloid imaging. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine.* May 2009;50(5):818-822.

**14.** Eli Lilly and Company, Amyvid Prescribing Information.

 Lilly USA, LLC, Indianapolis, p5. <http://pi.lilly.com/us/amyvid-uspi.pdf>.

**15.** O'Keefe GJ, Saunder TH, Ng S, et al. Radiation dosimetry of beta-amyloid tracers 11C-PiB and 18F-BAY94-9172. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine.* Feb 2009;50(2):309-315.

**XIII. BOARD OF DIRECTORS APPROVAL DATES:**

Version XX Month Day, 20xx