ACR–ACNM–ASNR–SNMMI PRACTICE PARAMETER FOR THE PERFORMANCE OF BRAIN PET/CT IMAGING IN DEMENTIA

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PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care[1]. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents 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 practitioner considering all the circumstances presented. Thus, an approach that differs from the guidance in this document, 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 this document when, in the reasonable judgment of the practitioner, such course of action is indicated by variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and 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 the guidance in this document will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The purpose of this document is to assist practitioners in achieving this objective.

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[1] *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing, 831 N.W.2d 826 (Iowa 2013) Iowa Supreme Court refuses to find that the "ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures (Revised 2008)" sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, Stanley v. McCarver, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.*

I. INTRODUCTION

This practice parameter was revised collaboratively by the American College of Radiology (ACR), the American College of Nuclear Medicine (ACNM), the American Society for Neuroradiology (ASNR), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

It is estimated that the number of people with dementia, which was 55 million worldwide in 2020, will almost

double every 20 years to 78 million in 2030 and to 139 million 2050, a result of changed demographics and increased longevity [1, 2]. This poses great challenges for both society and health care systems [3]. Three primary neurodegenerative etiologies of dementia are Alzheimer disease (AD),, frontotemporal lobar degeneration (FTLD), and dementia with Lewy bodies (DLB) [4]. AD is the most common form of dementia, accounting for approximately 60%–80% of all cases [2, 5].

The most prominent clinical feature of typical AD is an early impairment of episodic memory [6] which manifests as memory impairment for recent events, unusual repeated omissions, and difficulty learning new information. As the disease progresses, the symptoms often manifest in more persistent language disturbance and difficulties completing more complex tasks of daily living. The early stage of cognitive decline, namely, mild cognitive impairment (MCI), is the intermediate phase between normal cognition and dementia, during which patients show cognitive decline confirmed on objective cognitive testing but do not meet criteria for dementia because independent function is generally preserved [7]. Those with MCI convert to AD at a rate of approximately 10%–25% annually compared with healthy older individuals, who convert at a rate of approximately 1%–2% annually [4]. Approximately 20% of patients with MCI progress to other dementia types, and 30%–40% of cases do not progress to dementia [8].

The original diagnostic criteria for AD rested on the notion that AD is a clinical-pathological entity. The diagnosis was classified as definite (clinical diagnosis with histologic confirmation), probable (typical clinical syndrome without histologic confirmation), or possible AD (atypical clinical features but no alternative diagnosis apparent; no histologic confirmation). Possible AD can be identified when there is an atypical presentation or course but no evidence of an alternative or contributory pathology, such as prior significant head trauma, substance abuse, cerebrovascular disease, etc. A diagnosis of definite AD was made only according to criteria of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association when there was histopathologic confirmation of the clinical diagnosis [9].

With recent progress in research, distinctive biomarkers of the disease are now recognized including structural brain changes visible on magnetic resonance imaging (MRI), molecular imaging changes seen with positron emission tomography (PET), and changes in cerebrospinal fluid (CSF) biomarkers. These distinctive biomarkers have been incorporated into revised diagnostic criteria for underlying AD pathophysiology. These biomarkers can be divided into 3 major categories, reflecting the ATN framework of disease [10]:

1. Biomarkers of A-beta (Aß) amyloid accumulation in the brain, including abnormal radiopharmaceutical retention on amyloid PET imaging and low CSF Aß-42 peptide.
2. Biomarkers of tau pathology: abnormal tau deposition on tau PET imaging (flortaucipir).
3. Biomarkers of neuronal degeneration or injury: elevated total CSF tau protein; decreased ^{18}F fluorodeoxyglucose (FDG) uptake on PET in a specific topographic pattern involving posterior cingulate/precuneus and temporoparietal cortex; and atrophy on structural MR, again in a specific topographic pattern involving medial, basal, and lateral temporal lobes and medial and lateral parietal cortices [11].

Biomarkers of Aß amyloid are indicative of initiating upstream events that may deviate from normal before clinical symptoms manifest. Biomarkers of neuronal injury and neuronal dysfunction are indicative of downstream pathophysiological processes that temporally follow [11]. Current evidence suggests that amyloid biomarkers may become abnormal approximately 20 years before noticeable clinical symptoms but do not parallel clinical symptoms. The progression of clinical symptoms closely parallels the progressive worsening of neurodegenerative biomarkers (tau, atrophy, FDG) [7, 12, 13]. Biomarkers of neurodegeneration are now being incorporated into clinical diagnostic criteria for specific disorders, in particular for AD [14-16].

In 2004, CMS issued a positive coverage decision (NCD 220.6.13) for the use of FDG-PET to distinguish AD from frontotemporal dementia (FTD) [17]. It was determined that FDG-PET was reasonable and necessary only in patients with recent development of dementia who met diagnostic criteria for AD and FTD. The National Coverage Determination also contained a second and broader element for FDG-PET in the diagnosis of dementia under coverage with evidence development. FDA subsequently approved 3 amyloid PET radiopharmaceuticals (^{18}F-florbetapir, ^{18}F-Flutemetamol, ^{18}F-Florbetaben) for imaging of the brain for Aß-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for AD and other causes of cognitive decline.

A negative amyloid scan indicates sparse to no amyloid neuritic plaques and thus is not consistent with a neuropathological diagnosis of AD at the time of the scan. A negative scan reduces the likelihood that a patient's cognitive impairment is due to AD. A positive amyloid scan indicates moderate to severe amyloid neuritic plaques

and can be seen in AD, but also in patients with MCI and in older people with normal cognition who are at increased risk for progressing to MCI and AD [18].

In 2020, the FDA approved a single tau PET radiopharmaceutical (^{18}F-flortaucipir) for imaging tau neurofibrillary tangles in the brain parenchyma.

Postmortem studies indicate that the severity of neurodegeneration demonstrates a far better correlation with neurofibrillary tangle burden than Aβ-plaque load. Similar to FDG, tau-PET demonstrates a closer association with clinical severity and neurodegeneration, as compared with amyloid scans. Notably, the location and magnitude of tau accumulation on PET predicts future brain atrophy and neurodegeneration, compared with cortical amyloid deposition. Furthermore, increased tau uptake in disease-specific brain regions is associated with decreased cognitive performance. Therefore, tau-PET is an important predictor of cognitive change over time, and outperforms volumetric MRI and amyloid PET across the AD spectrum [19, 20].

This ACR practice parameter is for FDG, amyloid, and tau brain PET, PET/CT for patients with cognitive decline. For additional information on Definitions, see Appendix A.

II. INDICATIONS

A. FDG-PET

Imaging of regional glucose metabolism with the radiopharmaceutical FDG can provide unique neuronal metabolism information in patients with cognitive decline and dementia. Symptoms and signs of cognitive disorders are manifestations of synaptic and neuronal dysfunction and loss in neurodegenerative diseases. Regional patterns of altered glucose metabolism, as imaged with FDG-PET, can indicate the presence of a neurodegenerative process and can characterize involvement of individual cerebral structures and pathways. FDG-PET studies should be performed at the request of physicians knowledgeable in clinical diagnosis and management of dementia and under circumstances in which the examination results are likely to impact patient care. Examples of indications for FDG-PET imaging in cognitive decline and dementia include, but are not limited to, the following:

1. Assessment of progressive dementia: Although AD is the most common cause of dementia in elderly populations, several other neurodegenerative conditions exist that may be responsible for progressive dementia in the individual patient. FDG-PET may demonstrate characteristic regional patterns of cerebral hypometabolism, which could distinguish AD and AD subtypes from other degenerative processes such as those under the FTLD umbrella, DLB, and emerging pathologies including Limbic-predominant age-related TDP-43 encephalopathy, primary age-related tauopathy, argyrophilic grain disease, and fused in sarcoma [21].

2. Assessment of neurodegeneration in patients with MCI: Several studies support the utility of FDG-PET to identify patients with a course of progressive cognitive decline attributable to a neurodegenerative condition before the onset of clinically diagnosed dementia. Although the use of FDG-PET has not been determined to be useful for screening of asymptomatic patients who may ultimately be at risk of developing dementia, the modality can be useful in patients who meet the criteria for MCI [22-24].

B. Amyloid-PET

Clinical molecular imaging of cerebral fibrillar Aß-amyloid deposition is largely based on results obtained using the research radiopharmaceutical ^{11}C-Pittsburgh Compound-B and recent clinical trials used to support FDA approval of F-18–based amyloid imaging agents. The primary analysis of the Imaging Dementia – Evidence for Amyloid Scanning (IDEAS) study included 11,409 participants with MCI or dementia of uncertain cause. The patient management 90 days after amyloid PET changed (compared with the pre-PET plan) in 60.2% of patients with MCI and 63.5% of patients with dementia. Hence, amyloid PET was associated with changes in the subsequent management of diagnostically challenging patient cognitive disorders [25]. Furthermore, there was a change in diagnosis from AD to non-AD dementia or vice versa in more than a third of study participants. The etiologic diagnosis changed from AD to non-AD in 25.1% of

patients and from non-AD to AD in 10.5% of patients [25].
At present, clinical amyloid-PET imaging is not advised for use in screening asymptomatic patients with genetic or other risk factors for developing AD or in patients without a clinical diagnosis of a progressive cognitive decline or dementia as established by a clinician expert in the assessment and management of dementing disorders. In addition, amyloid PET cannot be used to establish the diagnosis of AD or monitor the response to therapy for AD in terms of disease progression or improvement, except as part of an approved clinical research trial of anti-amyloid therapy. A negative amyloid-PET study indicates absence of significant ß-amyloid plaques at the time of the study and does not exclude the future development of these plaques.

C. Tau-PET

Currently, there is a single FDA-approved agent targeting tau neurofibrillary tangles, ^{18}F-flortaucipir.

Tau-PET serves as a powerful predictive biomarker for AD progression, because it closely follows the hierarchical spreading pattern of neurofibrillary tangle pathology in a stepwise fashion; beginning in the entorhinal region, then spreading via the limbic and association areas, to the primary cortical areas [26]. Therefore, selective tau-PET not only provides important information on the neurobiology of AD but allows for examination of tau accumulation over time and its correlation with cognitive function, which leads to accurate assessments of disease severity and disease staging.

Given that the neuropathological diagnosis of AD requires the demonstration of the presence of both beta-amyloid neuritic plaques and tau neurofibrillary tangles in the brain parenchyma, the presence of tau deposition in β-amyloid positive patients together with a clinical evaluation allows for the establishment of a definitive diagnosis of AD antemortem.

Finally, measuring and monitoring tau load and its spread supports the development of tau-targeting disease-modifying therapies. Tau-PET is an indispensable tool for selecting patients for tau-targeting treatment trials, monitoring target engagement, and outcomes/effectiveness of anti-tau disease modifying therapies.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

A. Physician

PET/CT examinations of the brain should be performed under the supervision of and interpreted by a physician who meets qualifications outlined in the ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures [27].

AND

Initial Education and Experience

For brain FDG PET/CT:

1. Sufficient number of hours of CME in brain FDG PET/CT interpretation for dementia
2. Sufficient number of proctored or over-read brain FDG PET/CT scans performed for investigation of dementia before beginning unsupervised interpretation
3. Live or online education programs may be used to fulfill these requirements; this may also be fulfilled through a nuclear medicine residency or fellowship training program.

For amyloid PET/CT:

Sufficient number of hours of CME in brain amyloid PET/CT interpretation. Live or online educational programs may be used to fulfill this requirement. Interpretation of brain PET images to estimate ß-amyloid

neuritic plaque density should be performed only by readers who successfully complete a special training program such as one sponsored by the manufacturer of one of the FDA-approved radiopharmaceuticals. Live or online educational programs may be used to fulfill this requirement. There should be separate training for each separate FDA-approved PET brain amyloid radiopharmaceutical, which may have slightly different interpretation criteria. This may also be fulfilled through a nuclear medicine residency or fellowship training program.

For brain tau PET:

Sufficient number of hours of CME in brain tau PET interpretation. This can be achieved through live or online educational programs. Interpretation of brain PET images to assess tau pathology should be performed only by readers who complete a specialized training program, such as those sponsored by the manufacturers of FDA-approved radiopharmaceuticals. Live or online educational programs are acceptable for this requirement. This qualification may also be obtained through a nuclear medicine residency or fellowship training program.

Continuing Education and Experience
For continuing education and experience, please see the ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures [27] and ACR Practice Parameter for Continuing Medical Education (CME) [28].

B. Qualified Medical Physicist

For Qualified Medical Physicist qualifications, see the ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment [29].

C. Radiologic and Nuclear Medicine Technologist

See the ACR–SPR Practice Parameter for Performing and Interpreting Diagnostic Computed Tomography (CT) [30] and the ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures [27].

Representatives of the SNMMI and the American Society of Radiologic Technologists met in 2002 to discuss training technologists for PET/CT. The recommendations from that consensus conference for training technologists for PET/CT are outlined in the subsequent article published [31]. As a consequence of this conference and ensuing educational recommendations, cross-training and continuing educational programs have been developed to educate radiologic, radiation therapy, and nuclear medicine technologists in PET/CT fusion imaging.

The Nuclear Medicine Technology Certification Board (NMTCB) has developed a PET specialty examination that is open to appropriately educated and trained, certified, or registered nuclear medicine technologists, registered radiologic technologists, CT technologists, and registered radiation therapists, as defined on the NMTCB website (www.nmtcb.org). The American Registry of Radiologic Technologists (ARRT) offers a CT certification examination for qualified radiologic technologists and allows certified or registered nuclear medicine technologists who meet the educational and training requirements to take this examination. Eligibility criteria are located on the ARRT website (www.arrt.org).

D. Radiation Safety Officer

The radiation safety officer must meet the applicable requirements of the Nuclear Regulatory Commission for training as specified in 10 CFR 35.50 or equivalent state regulations.

IV. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for PET/CT of the brain should provide sufficient information to demonstrate the

medical necessity of the examination and allow for the proper performance and interpretation of the examination.

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

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state scope of practice requirements. (ACR Resolution 35 adopted in 2006 – revised in 2016, Resolution 12-b)

IV. SPECIFICATIONS OF THE EXAMINATION

A. Patient Preparation

1. For FDG PET/CT, the major goal of preparation is to minimize radiopharmaceutical uptake in normal tissues, such as the myocardium and skeletal muscle, while maintaining high FDG uptake in the brain. The preparation should include, but not be limited to, the following:
    a. Pregnancy testing when appropriate
    b. Fasting instruction (a minimum of 4-6 hours) and no oral or intravenous (IV) fluids containing sugar or dextrose
    c. Serum glucose analysis performed immediately before FDG administration (an optimal range is up to 200 mg/dL)
    d. Oral hydration to enhance renal excretion of FDG
    e. Focused history regarding the reason for examination (symptoms, diagnoses, and recent imaging examinations), treatments and medications, diabetes, and recent exercise. Patients should be injected in the awake resting state with eyes open while sitting or lying comfortably in a dimly lit and quiet room. The uptake of FDG when the patient's eyes are closed may cause hypometabolism in the occipital lobe, possibly leading to a misdiagnosis of DLB [32].
    f. Patients should be injected in the resting state while sitting or lying comfortably in a dimly lit and quiet room.
    g. Patients should void before being positioned on the PET/CT table. Patients can also be advised to void after completion of imaging to minimize radiation dose to the bladder and internal organs.

2. For ^{18}F-amyloid binding radiopharmaceutical PET/CT scan, the preparation should include, but not be limited to, the following:
    a. Pregnancy testing when appropriate
    b. Focused history regarding the reason for examination (symptoms, diagnoses, and recent imaging examinations) and treatments and medications. Oral hydration to enhance renal excretion of the radiopharmaceutical
    c. Patients should
    d. void before being positioned on the PET/CT table

3. For an ^{18}F-flortaucipir PET/CT scan, the preparation should include, but not be limited to, the following:
    a. Pregnancy testing when appropriate
    b. Focused history regarding the reason for examination (symptoms, diagnoses, and recent imaging examinations) and treatments and medications. Oral hydration to enhance renal excretion of the radiopharmaceutical
    c. Patients should
    d. void before being positioned on the PET/CT table

IV. SPECIFICATIONS OF THE EXAMINATION

B. Radiopharmaceutical

1. For ^{18}F-FDG, the amount of administered activity should be 185 to 296 MBq (5-8 mCi) IV.
2. For ^{18}F-amyloid binding radiopharmaceuticals, the amount of administered activity should be 185 to 740 MBq (5-12 mCi) IV. The recommended doses are 10 mCi, 5 mCi, and 8.1 mCi for florbetapir, flumetamol, and florbetaben, respectively [33-35].
3. For ^{18}F-flortaucipir, the amount of administered activity should be 370 MBq (10 mCi) IV.
4. Note: With PET/CT, the radiation dose to the patient is the combination of the administered activity from the PET radiopharmaceutical and the dose from the CT portion of the examination. Lower administered activities may be appropriate with longer imaging times and advances in PET/CT technology.

IV. SPECIFICATIONS OF THE EXAMINATION

C. Patient Positioning

1. Careful positioning of the patient's head in the center of the camera's field of view is important, although less critical in newer PET/CT scanners with long axial field of view or dedicated brain PET scanners.
2. The patient should be informed of the need to remain still throughout the scan, and a head holder may diminish movement artifacts. With patients with dementia, a comfortable head position may reduce motion artifacts.
3. Continuous supervision of the patient during the whole scanning procedure is necessary. This is especially important for patients with cognitive impairment.
4. Conscious sedation using a short-acting benzodiazepine for agitation may be needed in selected patients. Sedating medications should be given at least 20 minutes after radiopharmaceutical injection, preferably close to PET/CT acquisition.

IV. SPECIFICATIONS OF THE EXAMINATION

D. Protocol for CT Imaging

The CT performed as part of a PET/CT examination provides diagnostic information that may be relevant to both PET interpretation and overall patient care. A variety of protocols exist for performing the CT scan in the context of PET/CT scanning. In most cases, low-dose CT scans are used to provide attenuation correction and anatomic localization because the patient will often have an existing MR of the head. In patients in whom an MR is contraindicated, the CT portion of the examination can be performed as an optimized brain CT with standard brain CT imaging parameters if ordered by the referring physician. Regardless of the CT technique used, a careful review of CT images is necessary for comprehensive interpretation of the PET/CT examination. Patient positioning should be optimized to minimize radiation dose to the lens.

IV. SPECIFICATIONS OF THE EXAMINATION

E. Protocol for PET Imaging

1. A standardized acquisition protocol with a fixed acquisition start time is useful so that comparable data are obtained each time, whether from different patients or repeat scans in the same patient. PET emission acquisition should commence 35 to 60 minutes after FDG administration, 30–60 minutes after administration of ^{18}F-amyloid binding radiopharmaceutical, and 80 minutes after the administration of ^{18}F-flortaucipir. More specific details about the imaging protocol for individual amyloid PET radiopharmaceuticals can be found in the respective package inserts [33-35].
2. The duration of emission acquisition will depend on the performance characteristics of the individual scanner system, but a minimum of 10 minutes in 3-D mode is recommended. Twenty minutes is recommended for ^{18}F-flortaucipir.
3. PET data should be normalized for detector/geometric effects and corrected for random coincidences, dead time, scatter, and attenuation. Non–attenuation-corrected (NAC) images should also be reconstructed to assess patient motion.
4. If patient movement is a particular concern, the PET/CT scan can be performed as a dynamic acquisition (eg, five 2-minute frames). The dynamic images may be evaluated for motion, and the intact emission data may be combined before final reconstruction. List-mode acquisitions can be used for the same purpose.

5. Images should be reconstructed to have a pixel size less than 2 mm in the transverse plane.
6. Iterative or analytic reconstruction methods are acceptable, although consistent technique is important.
7. Reconstruction parameters depend on injected activity, scanner, acquisition parameters, available software, and the interpreting physician's preference.

IV. SPECIFICATIONS OF THE EXAMINATION

F. Interpretation

1. With an integrated PET/CT system, the software packages typically provide a comprehensive platform for image review.
2. A standard brain image review is recommended to ensure rapid, accurate, and reproducible interpretations. Internal landmark reorientation should be used to achieve standardized image display.
3. The images should be critically examined before interpretation for technical quality, especially evidence of movement. NAC PET images should be used to assess motion between CT and PET acquisitions.
4. Fused PET/CT images are helpful to identify motion and evaluate functional-structural findings simultaneously. Fusion of PET with MRI is desirable in all patients with dementia if an MRI brain is available.
5. Review of coronal and sagittal images is highly recommended.
6. Known morphological changes, such as atrophy, must be factored into interpretation of PET data.
7. Three-dimensional display of the data set (eg, by volume rendering or surface projections, such as 3-D stereotactic surface projection), can be helpful for the detection of lobar-specific disease patterns.
8. Comparison to an appropriate normative database (Z-score analysis) obtained under similar acquisition settings may improve diagnostic accuracy.
9. For amyloid PET/CT, image display and interpretation guidance from special training programs sponsored by the manufacturer of the FDA-approved radiopharmaceuticals needs to be followed because they vary between amyloid PET radiopharmaceuticals.
10. For tau PET/CT, image display and interpretation guidance from the manufacturer of the FDA-approved radiopharmaceutical needs to be followed.
11. Various methods for quantification of amyloid PET (Z-score analysis, SUVRs, Centiloid score) may be helpful for amyloid-PET interpretation, especially in equivocal cases.

V. EQUIPMENT SPECIFICATIONS

See the ACR–ASNR–SPR Practice Parameter for the Performance of Computed Tomography (CT) of the Head [36] and the ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment [29].

A. Performance Parameters

For patient imaging, the PET/CT scanner should meet or exceed the following specifications:

1. For the PET scanner
    a. In-plane spatial resolution: <6.5 mm
    b. Axial resolution: <6.5 mm
    c. Sensitivity (3-D): >4.0 cps/kBq
    d. Sensitivity (2-D): >1.0 cps/kBq
    e. Uniformity: 0.90-1.10 (recommended 0.95-1.05)

2. For the CT scanner (if applicable)
    a. Helical (spiral) scan time: <5 sec (<2 sec is preferable)
    b. Slice thickness and collimation: <5 mm (<2 mm is preferable)
    c. Limiting spatial resolution: >8 lp/cm for >32 cm display field of view (DFOV) and >10 lp/cm for <24 cm DFOV

B. Appropriate emergency equipment and medications must be immediately available to treat adverse

reactions associated with administered medications. The equipment and medications should be monitored for inventory and drug expiration dates on a regular basis. The equipment, medications, and other emergency support must also be appropriate for the range of ages and sizes in the patient population.

C. A fusion workstation with the capability to display PET, CT, and fused images with different percentages of PET and CT blending should also be available. Quantification software can be a useful adjunct to visual interpretation.

VI. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Parameter for Communication of Diagnostic Imaging Findings [37].

VII. EQUIPMENT QUALITY CONTROL

Equipment performance monitoring should be in accordance with the ACR–AAPM Technical Standard for Diagnostic Medical Physics Performance Monitoring of Computed Tomography (CT) Equipment [38].

PET/CT performance monitoring should be in accordance with the ACR–AAPM Technical Standard for Medical Physics Performance Monitoring of PET/CT Imaging Equipment [29].
Administered activity calibrator performance monitoring should be in accordance with the ACR–ACNM–SNMMI–SPR Practice Parameter for the Use of Radiopharmaceuticals in Diagnostic Procedures [27].
The accuracy of administered activity calibrators used for ^{18}F should ideally be measured using Germanium-68 (^{68}Ge) standards, cross-calibrated for ^{18}F and traceable to a national metrology lab.
Specific requirements for PET/CT brain imaging include quarterly testing with an ^{18}F fillable phantom, such as the ACR-approved PET phantom. Phantom images should be analyzed using the appropriate clinical workstations wherever possible. Qualitative assessment should include confirmation that PET and CT images are free from artifacts, particularly side-to-side gradients in intensity. The accuracy of the spatial registration of the PET and CT images should ideally be assessed quantitatively, although qualitative assessment is acceptable. The centers of the phantom inserts should be closely aligned on PET and CT with no systematic differences across the images. The uniform region of the PET images should have a standard uptake value in the range 0.9 to 1.1, with a target range of 0.95 to 1.05. Resolution recovery of the phantom inserts should be stable over time, and current measurements should be consistent with previous data, (eg, mean ± 2 SD of prior measurements).
A check of the performance of both the PET and CT components is required every day that the scanner is to be used and should be performed before patient imaging. The nature of these procedures will vary between scanners, and manufacturer recommendations should be followed. For PET, such tests should include verification of PET detector integrity, which involves a quantitative comparison of various detector parameters to reference values. Daily CT quality control should include a scan of a standard CT water phantom. The accuracy of the resulting CT numbers and image noise should be recorded.
When not indicated by the manufacturer's daily recommendations, a ^{68}Ge cylinder phantom is recommended for periodic assessment of PET/CT system stability. Additional use of this phantom is recommended after scanner maintenance or scheduled scanner recalibration and should be performed before patient imaging.
The dates and results of all quality control procedures should be recorded.

For specific issues regarding CT quality control, see the ACR–SPR Practice Parameter for Performing and Interpreting Diagnostic Computed Tomography (CT) [30].
For specific issues regarding PET and PET/CT quality control, see Section VII on Equipment Quality Control.

VIII. RADIATION SAFETY IN IMAGING

Radiologists, medical physicists, non-physician radiology providers**,** radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, "as low as reasonably achievable" (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel who work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection, application of dose constraints and limits) and the principles of proper management of radiation dose to patients (justification, optimization including the use of dose reference levels). https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1775_web.pdf

Facilities and their responsible staff should consult with the radiation safety officer to ensure that there are policies and procedures for the safe handling and administration of radiopharmaceuticals in accordance with ALARA principles. These policies and procedures must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC) and by applicable state, local, or other relevant regulatory agencies and accrediting bodies, as appropriate. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol, using body habitus or other customized method when such guidance is available.

Nationally developed guidelines, such as the ACR's Appropriateness Criteria®, should be used to help choose the most appropriate imaging procedures to prevent unnecessary radiation exposure.

Additional information regarding patient radiation safety in imaging is available from the following websites – Image Gently® for children (www.imagegently.org) and Image Wisely® for adults (www.imagewisely.org). These advocacy and awareness campaigns provide free educational materials for all stakeholders involved in imaging (patients, technologists, referring providers, medical physicists, and radiologists).

Radiation exposures or other dose indices should be periodically measured by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Monitoring or regular review of dose indices from patient imaging should be performed by comparing the facility's dose information with national benchmarks, such as the ACR Dose Index Registry and relevant publications relying on its data, applicable ACR Practice Parameters, NCRP Report No. 172, Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States or the Conference of Radiation Control Program Director's National Evaluation of X-ray Trends; 2006, 2009, amended 2013, revised 2023 (Res. 2d).

IX. RADIOPHARMACEUTICALS

A. FDG

^{18}F-FDG refers to a positron-emitting radiopharmaceutical containing radioactive 2-deoxy-2-(^{18}F) fluoro-D-glucose, which is used for diagnostic purposes in conjunction with PET. It is administered by IV injection. The active ingredient, 2-deoxy-2-(^{18}F) fluoro-D-glucose, abbreviated ^{18}F-FDG, has a molecular formula of $C_6H_{11}{}^{18}FO_5$ with a molecular weight of 181.26 Da. ^{18}F decays by positron ($ß^+$) emission and has a half-life of 109.7 minutes. The principal photons useful for diagnostic imaging are the 511 keV gamma photons, resulting from the annihilation of the emitted positron with an electron.

^{18}F FDG is taken up by cells and phosphorylated to ^{18}F-FDG-6-phosphate (^{18}F-FDG-6P) at a rate proportional to the rate of glucose utilization within a given tissue. ^{18}F-FDG-6P is not metabolized further in the glycolytic pathway (it is not a substrate for hexose phosphate isomerase) and is relatively trapped in the cell. In some cells, ^{18}F-FDG-6P may be dephosphorylated back to ^{18}F-FDG via glucose-6-phosphatase. This pathway is relatively minor in brain, skeletal muscle, and cardiac muscle, which permits PET imaging of the accumulated ^{18}F-FDG-6P in these target tissues. Many neoplasms have similar high phosphorylation to dephosphorylation rates, resulting in trapping of ^{18}F-FDG and retention of ^{18}F-FDG-6P. ^{18}F-FDG that is not involved in glucose metabolism is excreted unchanged in the urine.

B. Amyloid Radiotracers

The FDA has approved the use of 3 amyloid-avid radiotracers for human imaging of fibrillar amyloid deposition in the brain. A given tracer results in similar brain images with and without deposition [8].

^{18}F florbetapir is described as (E)-4-(2-(6-(2-(2-(2(18F) fluoroethroxy)ethoxy)ethoxy)pyridine-3-yl(vinyl)-N-methylbenzamine. The molecular weight is 359 [33].^{18}F flutemetamol is described as 2-(3-(18F)fluoro-4-(methylamino) phenyl)-6-benzothiazolol. It has the molecular formula C14H1118FN2OS. The molecular weight is 273.32[34].

^{18}F florbetaben is described as 4-((E)-2-(4-(2-(2-(2-(18F) fluoroethoxy)ethoxy)ethoxy)phenyl)vinyl)-N-methylaniline. The molecular weight is 358.45[35].

The time-activity curves for the amyloid tracers in the brains of subjects with positive scans are similar across the individual agents, showing continual signal increases from time zero through approximately 30 minutes after administration with stable values thereafter up to at least 90 minutes postinjection. Differences in the signal intensity between portions of the brain that specifically retain the amyloid tracer

and the portions of the brain with nonspecific retention form the basis of image interpretation. The specific binding of the radiotracers to Aß-amyloid aggregates was demonstrated in postmortem human brain sections using autoradiographic methods, thioflavin S, and traditional silver-staining correlation studies as well as monoclonal antibody Aß-amyloid–specific correlation studies. Radiotracer binding to tau protein aggregates and alpha-synuclein aggregates and a battery of neuroreceptors was not detected in invitro studies. Tracer-specific binding to fibrillar Aß-amyloid aggregates in vivo was confirmed for each of the tracers in comparison to autopsy measures of amyloid burden.

C. Tau targeted Radiotracer:

^{18}F-flortaucipir is described as 7-(6-fluoropyridin-3-yl)-5H-pyrido(4,3-b)indole. The molecular weight is 262.27, Flortaucipir is a radioactive diagnostic agent indicated for PET imaging of the brain to estimate the density and distribution of aggregated tau neurofibrillary tangles in adult patients with cognitive impairment who are being evaluated for AD [39].

X. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *ACR Position Statement on Quality Control and Improvement, Safety, Infection Control and Patient Education* on the ACR website (https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Quality-Control-and-Improvement).

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*Practice parameters and technical standards are published annually with an effective date of October 1 in the year in which amended, revised, or approved by the ACR Council. For practice parameters and technical standards published before 1999, the effective date was January 1 following the year in which the practice parameter or technical standard was amended, revised, or approved by the ACR Council.

Development Chronology for this Practice Parameter

2015 (Resolution 21)

Revised 2020 (Resolution 41)

Amended 2023 (Resolution 2c, 2d)

Revised 2025 (Resolution 21)

Appendix A

For the purpose of this practice parameter, the following definitions apply:

PET/CT scanner: A device that includes a single patient table for obtaining a PET scan, a CT scan, or both. If the patient stays reasonably immobile between the scans, the PET and CT data are aligned and can be accurately fused.

PET/CT acquisition: The process of collecting PET/CT data. In the context of brain imaging, data will be acquired from the vertex to the base of the skull. Typically this range will be encompassed by the axial field-of-view of the PET system, ie, no bed translation during PET data acquisition.

PET/CT registration: The process of taking PET and CT image sets that represent the same brain volume and aligning them such that there is a voxel-by-voxel match for the purpose of combined image display (fusion) or image analysis.

PET/CT fusion: The simultaneous display (superimposed or not) of registered PET and CT image sets. When superimposed, the image sets are typically displayed with the PET data color-coded onto the grayscale CT data.

PET/MRI scanner: A device that includes a single patient table for obtaining a PET scan and an MRI scan in a simultaneous manner.