

Alzheimer's Disease Neuro-Imaging III (ADNI3) Study

*PET Technical Procedures Manual: FDG (glucose metabolic imaging),
Florbetapir or Florbetaben (Amyloid Imaging), AV-1451 (Tau Imaging)*

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General Information

ADNI3 continues the currently funded AD Neuroimaging Initiative (ADNI2), a public/private collaboration between academia and industry to study biomarkers of AD. ADNI will inform the neuroscience of AD, identify diagnostic and prognostic markers, identify outcome measures that can be used in clinical trials, and help develop the most effective clinical trial scenarios. ADNI3 continues the aims of ADNI2 of amyloid PET imaging using [¹⁸F]-Florbetapir (Amyvid). In ADNI3, a second PET amyloid-imaging agent, [¹⁸F]-Florbetaben (Neuraceq) will be added in a subset of individuals. At the start of ADNI2, participants were also imaged for glucose metabolism with FDG; this was discontinued in the middle of ADNI2. [¹⁸F]-FDG-PET will be re-initiated at the baseline examination only for MCI and dementia participants. Finally, ADNI3 will also continue tau PET imaging with [¹⁸F]-AV1451 which was initiated as a pilot study in ADNI2. The schedule for tau PET imaging will vary according to amyloid status. All participants will receive a tau PET scan at baseline and again at the final visit. In addition, 20% of those who are amyloid negative, and 80% of those who are amyloid positive will receive 2 additional scans. Subject scan schedule will be communicated to the sites by ATRI.

Thus, the schedule for ADNI3 is that

- All subjects undergo amyloid PET with either florbetapir or florbetaben every 2 years
- All subjects undergo tau PET at start and end of study, with additional tau scans depending on amyloid status
- MCI and AD patients undergo FDG PET at baseline only

The purpose of this manual is to further explain the PET imaging component of the ADNI3 protocol. Standard procedures are needed to ensure consistency of data collection in this longitudinal study.

This manual contains information for study-site clinical staff involved with the care of study subjects during the imaging procedure and those involved with the processing and transfer of PET imaging data.

All PET scans must be completed within 2 weeks before or 2 weeks after the in-clinic assessments at two-year intervals through the life of the ADNI3 grant for CN, MCI and AD cohort.

Contact Information

PET protocol & image upload

General PET Questions

adni-pet-l@usc.edu

For general PET-related questions or concerns regarding the overall imaging protocol.

Uploading to LONI

adni@loni.usc.edu

For question regarding the scan uploading to the LONI website.

(For questions/concerns regarding individual subjects contact the study coordinator at your referral site).

Technical/QC questions

koepp@umich.edu (Robert A. Koeppe)

For questions regarding scanner specific acquisition and reconstruction parameters.

Visit scheduling and general study related inquiries

adni-study@usc.edu

Florbetapir F 18 (Amyvid) / ¹⁸F-AV-1451 (Flortaucipir) ordering

Avid Radiopharmaceuticals

clinicalsupply@avidrp.com

Florbetaben (Neuraceq) ordering

Piramal Radiopharmaceuticals

Neuraceq.Orders@piramal.com

Site Qualification

PET Scanners

It is preferable for sites to use existing qualified ADNI scanners for PET imaging. If a new scanner must be introduced it will need to be qualified using standard ADNI scanner qualification before imaging can be performed. (Contact: koepp@umich.edu)

Ideally, no hardware or software upgrades of the PET imaging system should occur during the duration of the study. In the event of such an upgrade, we ask that you inform the PET core **prior** to the anticipated upgrade. Depending on the nature of the upgrade the site may be asked to repeat the phantom scans prior to scanning any additional subjects.

Contact adnipet@ucsd.edu prior to imaging if a new scanner will be used for ADNI3 or if hardware / software upgrades have occurred.

Regulatory

Sites must be appropriately licensed through appropriate state or federal agencies to receive and use all radiotracers prior to imaging.

Sites must also receive both **IRB** approval and **radiation safety committee (RSC) or similar** approval, before scanning any subjects. The current protocol for ADNI3 contains radiation dosimetry and all information relevant to study procedures for review by the IRB and RSC.

Continued Quality Monitoring During Execution Phase

To ensure scanner/ancillary equipment stability and quality throughout the project, each site is required to perform ongoing quality control procedures.

Dedicated PET Scanner:

- PET scanner should have an up to date calibration and normalization on the date of each imaging session.
- A daily QC/blank scan should be done at the beginning of the day the scanning is to be completed. This scan should be visually inspected for abnormalities. If there is a possibility that the abnormality could impact the quality of the PET scan the study should be rescheduled.

PET/CT Scanner:

- PET scanner should have an up to date calibration and normalization on the date of the imaging session.
- A daily QC check should be done at the beginning of the day the scanning is to be completed. This scan should be visually inspected for abnormalities. If there is a possibility that the abnormality could impact the quality of the PET scan the study should be rescheduled.
- Daily CT should be performed as recommended by the specific vendor, but typically should include a "checkup/calibration" procedure and a water phantom scan. The checkup/calibration procedure guarantees optimum image quality by warming up the x-ray tube and should be performed at startup and within 1 hour prior to any scan. The water phantom provides quality measurements of 3 parameters. The parameters are the CRT value of water calculated in Hounsfield units (HU), the pixel noise of images calculated as a standard deviation, and the tube voltages measured directly on the x-ray tubes. These three measurements should be determined for all available KVP values.

PET/MR Scanners

- Are not permitted in ADNI3

Ancillary Equipment:

- Quality control of the dose calibrator should be performed throughout the course of the study. This typically will include daily constancy, quarterly linearity checks and annual accuracy tests

PET Pre-Scan Procedures / General Information

Subject Pre-screening

All subjects should have been screened by the study coordinator for the following contra-indications:

- Conditions that, in the investigator's opinion, could increase the risk to the participant, limit the participant's ability to tolerate the experimental procedures or interfere with collection/analysis of the data (for example, participants with severe chronic back pain might not be able to lie still during the scanning procedures).
- Abnormal findings on the physical examination or laboratory screening tests that suggest the patient might have a condition that could, in the opinion of the investigator, affect his or her response to the radiopharmaceutical and related testing procedures.

- Inability to cooperate/claustrophobia (sedation is not offered for this protocol)
- Inability to lie on the scanner bed for 30-40 minutes

Florbetapir (Amyvid) Ordering

Study coordinators and PET technologists will need to reference the Avid Radiopharmaceuticals, Inc. **Clinical Supplies Guidance Document (CSGD)** for all relevant documents regarding ordering, shipping and receiving unit doses of florbetapir F 18 (Amyvid™). Study coordinators will coordinate Florbetapir ordering with the PET imaging facility using the Florbetapir drug request form (DRF). Doses typically require a minimum of a 5-day notification **prior** to the desired day of imaging to coordinate production and delivery. The Avid clinical supply manager will work with the study coordinator to ensure a comparable injection time is agreed upon.

Florbetaben (Neuraceq) Ordering

Study coordinators and PET technologists will need to reference the Piramal Imaging supply documents for all relevant information regarding ordering, shipping and receiving unit doses of Florbetaben (Neuraceq™). Study coordinators will coordinate Florbetaben ordering with the PET imaging facility using the florbetaben drug request form (DRF). Doses require a minimum of a 2-day notification **prior** to the desired day of imaging to coordinate production and delivery. The Piramal Imaging clinical supply manager (Neuraceq.Orders@piramal.com and Amit Kumar, amit.kumar@piramal.com) will work with the study coordinator to ensure a comparable injection time is agreed upon.

AV-1451 (Flortaucipir) Ordering

Study coordinators and PET technologists will need to reference the Avid Radiopharmaceuticals, Inc. Clinical Supplies Guidance Document (CSGD) for all relevant documents regarding ordering, shipping and receiving AV-1451 for injection. Study coordinators will coordinate AV-1451 ordering with the PET imaging facility using the AV-1451 drug request form (DRF). Avid typically require a 5-day notification prior to the desired day of imaging to coordinate production and delivery.

FDG Ordering

Each site is responsible for producing or purchasing its own FDG, as has been the case in both ADNI1 and ADNI2.

Subject Dietary Restrictions

Florbetapir / Florbetaben Scans / AV-1451 Scans:

There are no specific dietary restrictions for the florbetapir, florbetaben or AV-1451.

FDG Scans:

Subjects to be imaged in the morning are asked to omit all food and fluids (except water) from midnight the night before the scan until after the imaging is completed. Subjects scanned later in the day are asked to omit food and fluids (except water) for at least 4 hours prior to the imaging session.

Subject Positioning

Proper subject positioning is a key aspect of the successful completion of the PET exams. It is important to take the time necessary to ensure not only that the subject is properly positioned but also can comfortably maintain that position throughout the duration of the scanning session. **Excessive motion and in particular a difference in the subjects' position between the emission scan and the transmission or CT scan used for attenuation correction is the single most common cause of failed studies.**

- Have the subject remove any bulky items from their pockets such as billfolds, keys, etc. In addition, they should remove eyeglasses, earrings, and hair clips/combs if present. If possible they should try and remove hearing aids also.
- Position the subject so that their head and neck are relaxed. It may be necessary to add additional pads beneath the neck to provide sufficient support. Use the lasers to ensure there is little or no rotation in either plane. The head should be approximately positioned such that the PET scanning planes are parallel to the imaginary line between the external canthus of the eye and the external auditory meatus (orbitomeatal plane) and the head is centered in the sagittal plane. More important exact matching of the orbitomeatal plane is making sure the subject is comfortable, which will hopefully translate to less subject motion during the scan.
- Use support devices under the back and/or legs to help decrease the strain on these regions. This also will assist in the stabilization of motion in the lower body.
- Once the subject has been positioned foam pads can be placed alongside the head for additional support. Velcro straps and/or tape should also be used to secure the head position. Vacuum beanbags can also be used in this process.
- The subjects should be offered a “panic button” or be reassured that someone is watching or able to hear them at all times.

- **Proper positioning of the subject to get the entire head in the field of view is critical to the success of the project.**
- Checking the subject positioning and readjusting (if possible) the position of the subjects' head should be done often throughout the study.

Ambient Conditions

Standardization of the environment during the uptake period following **Florbetapir**, **Florbetaben**, or **AV-1451** administration is not essential.

FDG Scans:

Standardization of the environment during the first 20-25 minutes following **FDG** administration is essential.

- During the uptake phase, subjects should be asked to remain still and keep awake with eyes open looking straight ahead (not into lights).
- Lights should be dimmed to a level similar to twilight. The subjects' position (e.g., sitting or lying), their visual environment, and the room's ambient light should be the same throughout the longitudinal study.
- The subject should be monitored periodically to be certain of compliance and to ensure that the eyes do not close and the subject remains awake.

Image File Identification

It is VERY important that each site follow standard file identification so that all scans can be easily identified. The Clinical Study Coordinator at the clinical site prior to the PET visit will assign the file ID. The naming convention is xxx_S_yyyy where xxx is the three-digit site ID, and yyyy is the unique four-digit subject ID assigned by ATRI. The “_S_” stands for ‘Subject’. If uploading phantom data, please use “_P_” (for Phantom) For example, 129_S_4412 is the subject enrolled in ADNI with ID 4412 and is from site 129.

IMPORTANT: It is important to ensure in the series description, the type of PET scan (radiotracer) is identified as either florbetapir (amyvid; AV45), florbetaben (Neuraceq), FDG, or AV-1451

Documentation

The study coordinator must ensure the PET Technologist has a copy of all PET Scan Information Forms prior to each scan session, and that the PET scan information form

matches the type of study being performed (amyloid, tau, or glucose metabolism). Be sure to complete the metadata sheet as the study is being acquired. A process should be established for transferring this form(s) back to the study coordinator. **The study coordinator will then need to ensure the appropriate data is entered online within 24 hours of the scan.**

PET Procedures

- Have the subject use the restroom and empty their bladder.
- Allow them to lie comfortably in a bed or reclining chair in a room. Supply them with blankets/pillows as needed to maximize their comfort.
- Obtain intravenous access using a small angiocath.
- Inspect the radiopharmaceutical dose solution prior to administration and do not use it if it contains particulate matter or is discolored.

Radiotracer Doses:

- Using aseptic technique and radiation shielding, draw of the radiotracer and assay with a dose calibrator. Record the assay time to the nearest minute. Do not add saline to the dose prior to administration. Adding saline could potentially lead to precipitation out of solution form.

Radiotracer doses:

Florbetapir (Amyvid):	370 MBq (10.0 mCi) ± 10%
Florbetaben (Neuraceq):	300 MBq (8.1 mCi) ± 10%
AV-1451:	370 MBq (10.0 mCi) ± 10%
FDG:	185 MBq (5.0 mCi) ± 10%

The above are target doses. Scans should never be performed using doses greater than 10% above the target dose. Every attempt should be made to perform the study with 10% of the target dose. If insufficient activity is available to achieve the target range, scans may be performed down to 50% of the target dose. PET scans must not be performed with doses below the following minimum injectable dose:

Minimum injectable doses: Florbetapir - 185 MBq (5.0 mCi);
Florbetaben 150 MBq (4.1 mCi); AV-1451 - 185 MBq (5.0 mCi);
FDG - 93 MBq, (2.5 mCi)

- **Draw up sufficient tracer to achieve the target dose** and assay with a dose calibrator.
- **Record the assay time to the nearest minute.** Do not q.s. (add saline) to the dose prior to administration. Adding saline could potentially lead

to precipitation out of solution form.

- Inject the radiotracer and follow the injection with an intravenous flush of 0.9% sterile sodium chloride. **Record the injection time to the nearest minute.** The IV line can be discontinued at this time.
- Re-assay the dose syringe. If the residual activity is 0.1 mCi or greater, record the amount and correct the amount of the injected dose for the residual activity.
- Allow the subject to rest comfortably in the room during the incorporation period until about 10-15 min prior to the start time for the particular radiotracer.
- At this time, have the subject use the restroom and empty their bladder.
- For PET/CT scanners, the subject should be placed on the scanning table early enough to obtain a CT scan prior to the emission scan, and still be able to begin the emission acquisition at the appropriate start time. **PET-only systems will acquire a transmission scan following the emission acquisition**, so preparation of the subject can begin a few minutes later than if on a PET/CT system.
- Position and secure the subject in the scanner. Alignment marks should be put on the subject using the laser system, which can then be subsequently used to check alignment and reposition the subject as necessary.

Attenuation Correction Procedures:

PET/CT Scanners

- Standard CT acquisition parameters, but low effect mAs (~30 is typical)
- The subject must undergo the CT scan starting about 5 minutes prior to starting the PET scan. Be sure to prepare the subject so that you are ready to press “start” for the PET emission scan at the required time.

PET Only Scanners

- Acquire an attenuation correction scan using rod sources for 5-6 minutes after the acquisition of the standard emission scan. The subject should be repositioned “on their marks” prior to acquiring the transmission scan.
- Segmentation and re-projection routines will be applied for attenuation correction.

PET Scan Procedures:

Amyloid scans:

- IV injection of amyloid tracer:
 - **Florbetapir** (Amyvid) **370 MBq (10.0 mCi) ± 10%**
 - **Florbetaben** (Neuraceq) **300 MBq (8.1 mCi) ± 10%**
- All subjects will have a **20-minute** continuous brain PET imaging that will begin at either **50 minutes** (florbetapir) or **90 minutes** (florbetaben) post-injection. Scans should never be started prior to the 50 or 90 min start time; and every effort must be made to start the scan on time. Scheduling scans very close in time following a clinical study (which could run late) is not an acceptable reason for starting a scan late.
- Emission acquisition start time:
 - Florbetapir (Amyvid) **50 min**
 - Florbetaben (Neuraceq) **90 min**
- Acquire a **20 min dynamic scan** consisting of **four 5-minute frames**. **Acquisition should start promptly at 50 or 90 minutes post injection, depending on the tracer.** Scans should never be started prior to 50 or 90 min; and every effort must be made to start the scan on time. Scheduling an ADNI PET scan very close in time following another study (which could run late) is not an acceptable reason for starting a scan late.
- It is crucial that the subject's position is checked several times throughout the 20-min PET scan. A good idea is to check the subject's marks using the laser system at the end of each 5 min scan frame. The subject's position should be returned as closely as possible to the original position just at the beginning of the next scan frame.

AV-1451 tau PET scans

- The following assessments will be performed for all participants:
 - A physician or a licensed/credentialed medical professional (i.e., a PET technologist, imaging center nurse or regional equivalent) designated by the site principal investigator, must assess or evaluate the subject prior to administration of AV-1451 injection to determine if they are still suitable to undergo the scan. If a designee performs this activity, a physician must be available to provide medical consultation.
 - ECG with results reviewed prior to AV-1451 dose administration.

- Adverse events (AEs) will be continuously monitored during the AV-1451 imaging session. Subjects who experience an AE will not be discharged from the imaging center until the event has resolved or stabilized.
- Injection of Tau tracer:
 - **AV-1451 370 MBq (10.0 mCi) ± 10%**
- Acquire a **30 min dynamic scan** consisting of **six 5-minute frames**. **Acquisition should start promptly at 75 minutes post injection.** Scans should never be started prior to 75 min; and every effort must be made to start the scan on time. Scheduling an ADNI PET scan very close in time following another study (which could run late) is not an acceptable reason for starting a scan late.
- It is crucial that the subject's position is checked several times throughout the 30-min PET scan. A good idea is to check the subject's marks using the laser system at the end of each 5 min scan frame. The subject's position should be returned as closely as possible to the original position just at the beginning of the next scan frame.
- Post AV-1451 scan:
 - The subject will be requested to void after completion of the PET scan.
 - A physician or a licensed/credentialed medical professional (i.e., a PET technologist, imaging center nurse or a regional equivalent) designated by the site principal investigator must assess or evaluate the subject prior to discharge from the imaging center to evaluate the subject's readiness for discharge. If a designee performs this activity, a physician must be available to provide medical consultation.
 - A follow-up phone call to the subject should be conducted between 2 or 3 business days of the imaging day, but not before 48 hours post-injection, to confirm subject well-being and to collect information about any new adverse events.

FDG PET Scans:

- Upon arrival to the imaging center, compliance to the dietary requirements should be confirmed. If they have not complied with the preparation instructions then the following procedures should apply:
 - If < 2 hours have elapsed since food/drink, wait until 2 hours have elapsed from last ingestion.

- Once >2 hours have elapsed since last ingestion, measure the blood glucose levels. If the blood glucose level is <180 mg/dL (9.9 mmol/L) then proceed with the scan. If not, the subject will need to wait an additional amount of time until the blood glucose levels meet the above criteria or reschedule.
- Injection of glucose metabolism tracer:
 - **FDG 185 MBq (5.0 mCi) ± 10%**
- Acquire a **30 min dynamic scan** consisting of **six 5-minute frames**. **Acquisition should start promptly at 30 minutes post injection.** Scans should never be started prior to 30 min; and every effort must be made to start the scan on time. Scheduling an ADNI PET scan very close in time following another study (which could run late) is not an acceptable reason for starting a scan late.
- It is crucial that the subject's position is checked several times throughout the 30-min PET scan. A good idea is to check the subject's marks using the laser system at the end of each 5 min scan frame. The subject's position should be returned as closely as possible to the original position just at the beginning of the next scan frame.
- Post FDG scan: The subject will be requested to void after completion of the PET scan.

Post PET Scan:

- Reconstruct images using parameters specific to the system used for scanning (See Appendix B). The same reconstruction parameters should be used for all emission scans. Upon completion of the reconstruction, review all the images to assess for artifacts.
- Archive ALL raw and processed study data including copies of the normalization and blank scans. It is necessary to archive and store raw and processed data at the imaging site for the duration of the project (approximately 5 years).
- Transfer image data to the Laboratory of Neuroimaging (LONI) at USC. Please upload only the fully corrected image set.

IMPORTANT: Data uploads to LONI should be performed as soon as the images have been acquired & reconstructed as it will be important to promptly QC the data to identify if the scan needs to be repeated. The time frame should be 1-2 business days from acquisition

Appendix A – LONI Access User Registration

USER REGISTRATION

Please refer to the separate LONI document “IDA Image Archive” for instructions on LONI account generation and image uploads. Posted to ADNI3 study document materials folder in Box.

Appendix B – Scanner Specific Reconstruction Parameters

This appendix outlines the reconstruction parameters for the FDG, Florbetapir, florbetaben and AV-1451 scans

GE sites: please note that secondary reconstructions for GE scanners using 3-D back projection are no longer needed. Thank you to those sites that have been providing the extra reconstructions during ADNI-2.)

**For questions regarding scanner specific reconstruction parameters:
Email Robert Koeppe (koeppe@umich.edu)**

GE Discovery 600, 610, 690, and 710 - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six \wedge 5-min frames

Florbetapir F-18: 20 min, four \wedge 5-min frames

Florbetaben: 20 min, four \wedge 5-min frames

AV-1451: 30 min, six \wedge 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method:

3D Iterative (fully 3D Iter; not 3D FORE iterative IR):

4 iterations; 24 subsets (or as close to 24 subsets as the software allows)

Grid: 192 \wedge 192 \wedge 47

FOV: 256 mm (results in voxel size of 1.333 mm)

Slice Thickness: 3.27 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

GE Discovery STE - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method: Iterative (fully 3D Iter; not 3D FORE IR):
4 iterations; 20 subsets

Grid: 128 ^ 128

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 3.27 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

GE Discovery ST - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir F-18: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start given immediately above. Scans should never be started early.

Scans and scan duration:

FDG: 30 min, six \wedge 5-min frames

Florbetapir F-18: 20 min, four \wedge 5-min frames

Florbetaben: 20 min, four \wedge 5-min frames

AV-1451: 30 min, six \wedge 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method: Iterative if available (fully 3D Iter; not 3D FORE IR) Only if fully iterative is not available, as in some older systems, is it ok to use 3D FORE IR.

4 iterations; 21 subsets* (* for older software versions having only 3D FORE IR, **24 subsets**)

Grid: 128 \wedge 128 \wedge 47

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 3.27 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

GE Discovery STE - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method: Iterative (fully 3D Iter; not 3D FORE IR): 4 iterations; 21 subsets

Grid: 128 ^ 128

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 3.27 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

GE Discovery LS - 35 slice (PET/CT) scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method: FORE Iterative:

4 iterations; 21 subsets

Grid: 128 ^ 128 ^ 47

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 4.25 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

GE Advance - 35 slice PET scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six \wedge 5-min frames

Florbetapir F-18: 20 min, four \wedge 5-min frames

Florbetaben: 20 min, four \wedge 5-min frames

AV-1451: 30 min, six \wedge 5-min frames

Randoms Correction:

Singles: (not real-time subtraction)

Reconstruction Parameters:

Reconstruction Method: FORE Iterative: 4 iterations; 21 subsets

Grid: 128 \wedge 128 \wedge 47

FOV: 256 mm (results in voxel size of 2.0 mm) Slice Thickness: 4.25 mm

Smoothing Filter: NONE or 0.0 (for all filter options: loop filter, post-filter and z-axis filter)

All corrections 'On'

Note: Reconstruction offsets should be used to assure the head is fully in the in-plane FoV.

Philips Ingenuity TF - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Acquisition Protocol: Brain

Reconstruction Parameters:

Reconstruction Method: Blob-OS-TF

Grid: 128 ^ 128 ^ 90

FOV: 256 mm (results in voxel size of 2.0 mm) Slice Thickness: 2.0 mm

Smoothing: Set SMOOTHING parameter to 'SHARP'

All other parameters should be set to defaults for the "Brain" protocol. All corrections 'On'

For Blob-OS-TF reconstruction: The attenuation field should indicate "CTAC-SG" and the scatter field should indicate "SS-Simul".

Philips Gemini TF - PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan: Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Acquisition Protocol: Brain Protocol

Reconstruction Parameters:

Reconstruction Method: Iterative: LOR-Ramla

Grid: 128 ^ 128 ^ 90

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 2.0 mm

Smoothing: Set SMOOTHING parameter to 'SHARP'

All other parameters should be set to defaults for the "Brain" protocol. All corrections 'On'

For LOR-Ramla reconstruction: The attenuation field should indicate "CTAC-SG" and the scatter field should indicate "SS-Simul".

Philips Gemini and Gemini GXL - 90 slice PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Acquisition Protocol: Brain Protocol

Reconstruction Parameters:

Reconstruction Method: Iterative: LOR-Ramla

(*** Note: if only older software versions are available, 3D Ramla reconstruction is acceptable)

Grid: 128 ^ 128 ^ 90

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 2.0 mm

Smoothing: Set SMOOTH parameter to 'SHARP'

(**Note: for older software with RAMLA-3D reconstruction, the 'smoothing' is governed by the parameter lambda, which should be set to a value of 0.008)

All other parameters should be set to defaults for the "Brain" protocol

All corrections 'On'

For LOR-Ramla reconstruction: The attenuation field should indicate "CT-SEG" and the scatter field should indicate "SS-Simul"

Philips Allegro - 90 slice PET scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Transmission scan:

Florbetapir: Five or six min 2-D scan acquired immediately **post**-emission scan; process with segmentation.

Acquisition Protocol: Brain Protocol

Reconstruction Parameters:

Reconstruction Method: Iterative: LOR 3D Ramla

(*** Note: if only older software versions are available, 3D Ramla reconstruction is acceptable)

Grid: 128 ^ 128 ^ 90

FOV: 256 mm (results in voxel size of 2.0 mm)

Slice Thickness: 2.0 mm

Smoothing: Set SMOOTH parameter to 'SHARP'

(**Note: for older software with 3D-RAMA reconstruction, the smoothing is governed by the parameter lambda, which should be set to a value of 0.008)

All other parameters should be set to defaults for the "Brain" protocol

All corrections 'On'

For LOR-Ramla reconstruction: The attenuation field should indicate "CT-SEG" and the scatter field should indicate "SS-Simul"

Siemens BioGraph mCT - mCT TrueV PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

LIST-MODE: If your scanner has list-mode capability:

FDG: 30 min, six \wedge 5-min frames

Florbetapir F-18: 20 min, four \wedge 5-min frames

Florbetaben: 20 min, four \wedge 5-min frames

AV-1451: 30 min, six \wedge 5-min frames

NO LIST-MODE: ONLY If your scanner does not have list-mode capability:

Florbetapir and florbetaben: **Two scans: 10-min each**

FDG and AV-1451: **Two scans: 15-min each**

*** Note that reduce motion artifacts, two separate emission scans will be acquired as closely together as possible. Do not repeat CT scan.

Reconstruction Parameters:

Method: Iterative: OSEM-3D (do NOT use TrueX or ToF reconstruction)
4 iterations; 24 subsets

Grid: 400 \wedge 400 \wedge 81 (or 109 for TrueV model)

Zoom: 2.0 (results in voxel size of ~1.018 mm)

Smoothing Filter: NONE (All-pass or '0.0')

Match CT: 'Off' or 'No' (results in PET slice thickness of ~2.027 mm) All corrections 'On'

Siemens BioGraph TruePoint – and TruePoint TrueV PET/CT scanners (Models 1093, 1094)

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

LIST-MODE: If your scanner has list-mode capability: FDG: **30 min, six ^ 5-min frames**

Florbetapir F-18: **20 min, four ^ 5-min frames**

Florbetaben: **20 min, four ^ 5-min frames**

AV-1451: **30 min, six ^ 5-min frames**

NO LIST-MODE: ONLY If your scanner does not have list-mode capability:

Florbetapir and florbetaben: **Two scans: 10-min each**

FDG and AV-1451: **Two scans: 15-min each**

*** Note that reduce motion artifacts, two separate emission scans will be acquired as closely together as possible. Do not repeat CT scan.

Reconstruction Parameters:

Method: Iterative: OSEM-3D (do NOT use TrueX reconstruction)

4 iterations; 21 subsets

Grid: 336 ^ 336 ^ 81 (or 109 for TrueV (1094) model)

Zoom: 2.0 (results in voxel size of ~1.015 mm)

Smoothing Filter: NONE (All-pass or '0.0')

Match CT: 'Off' or 'No' (results in PET slice thickness of ~2.027 mm) All corrections 'On'

Siemens BioGraph HiRes - 81 slice PET/CT scanners (Model 1080)

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time given immediately above. Scans should never be started early

Scans and scan duration:

LIST-MODE: If your scanner has list-mode capability:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

NO LIST-MODE: ONLY If your scanner does not have list-mode capability:

Florbetapir and florbetaben: **Two scans: 10-min each**

FDG and AV-1451: **Two scans: 15-min each**

*** Note that reduce motion artifacts, two separate emission scans will be acquired as closely together as possible. Do not repeat CT scan.

Reconstruction Parameters:

Method: Iterative: FORE / OSEM-2D 4 iterations; 16 subsets

Grid: 168 ^ 168 ^ 81

TRIM: 'On'

Zoom: 2.0 (results in voxel size of ~2.03 mm)

Smoothing Filter: NONE (All-pass or '0.0') Match CT Slice

All location: 'Off' or 'No' (results in PET slice thickness of ~2.00 mm)

All corrections 'On'

Siemens ECAT Exact HR+ (BGO) 63-slice scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Transmission scan:

Five or six min 2-D scan acquired immediately post-emission scan; process with **segmentation**.

Reconstruction Parameters:

Method: Iterative: (FORE / OSEM-2D) 4 iterations; 16 subsets

Grid: 128 ^ 128 ^ 63

Brain Mode: ON

Zoom: 2.0

Smoothing Filter: NONE (software version 7.2 says 'All Pass (Ramp)')

Axial filtering: NONE (software version 7.2 says 'Off')

All corrections 'On'

Siemens HRRT 207-slice PET-only scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

Scans and scan duration:

FDG: 30 min, six \wedge 5-min frames

Florbetapir F-18: 20 min, four \wedge 5-min frames

Florbetaben F18: 20 min, four \wedge 5-min frames

AV-1451: 30 min, six \wedge 5-min frames

Transmission scan: Five or six min scan acquired immediately **post**-emission scan.

Reconstruction Parameters:

Method: Iterative: (OP OSEM-3D) 6 iterations; 16 subsets

Grid: 256 \times 256 \times 207 Voxel size: 1.219 mm³

Smoothing Filter: 2mm Gaussian All corrections 'On'

Siemens BioGraph (LSO; Models 1023,1024) 47-slice PET/CT scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

CT Scan:

Low mAs scan acquired shortly before emission. Leave enough time to start emission acquisition promptly at start time giving immediately above. Scans should never be started early

Scans and scan duration:

Florbetapir and Florbetaben: **Two scans: 10-min each**

FDG and AV-1451: **Two scans: 15-min each**

*** Note that to reduce motion artifacts, two separate emission scans will be acquired as closely together as possible. If your scanner software version does not allow a repeat emission acquisition unless you perform a second CT scan, please contact Robert Koeppel (see below) prior to scanning

Reconstruction Parameters:

Method: Iterative: (FORE / OSEM-2D) 6 iterations; 16 subsets

Grid: 128 \times 128 \times 47

TRIM: ON

Zoom: 2.0

Smoothing Filter: NONE (or '0.0')

All corrections 'On'

If your scanner software version has an option for "Match CT Slice location", this must be left 'OFF' (e.g. box is unchecked)

Siemens ECAT Exact (BGO) and Accel (LSO) 47-slice PET-only scanners

Acquisition Parameters:

Radiotracer:

FDG: 5 mCi ($\pm 10\%$)

Florbetapir: 10 mCi ($\pm 10\%$)

Florbetaben: 8.1 mCi ($\pm 10\%$)

AV-1451: 10 mCi ($\pm 10\%$)

Scan start time post-injection:

FDG: 30 min

Florbetapir: 50 min

Florbetaben: 90 min

AV-1451: 75 min

Scans and scan duration:

FDG: 30 min, six ^ 5-min frames

Florbetapir F-18: 20 min, four ^ 5-min frames

Florbetaben: 20 min, four ^ 5-min frames

AV-1451: 30 min, six ^ 5-min frames

Transmission scan:

Five or six min 2-D scan acquired immediately post-emission scan; process with **segmentation**.

Reconstruction Parameters:

Method: Iterative: (FORE / OSEM-2D) 6 iterations; 16 subsets

Grid: 128 ^ 128 ^ 47

Brain Mode: ON

Zoom: 2.0

Smoothing Filter: NONE (software version 7.2 says 'All Pass (Ramp)')

Axial filtering: NONE (software version 7.2 says 'Off') All corrections 'On'

**For questions regarding scanner specific reconstruction parameters:
Email Robert Koeppe (koeppe@umich.edu)**