

**Dominantly Inherited Alzheimer Network (DIAN)
PET Technical Procedures Manual**

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A. Imaging Overview:

We hypothesize that Alzheimer's disease (AD) has a preclinical stage in which elevated levels of brain amyloid protein and accumulation of beta-amyloid deposits foreshadow the gradual onset of neuronal dysfunction, cell loss and dementia. While the exact role of amyloid in the initiation of brain damage is still unclear, we suggest that clarifying the temporal relationships between amyloid deposition, neural dysfunction and loss, and the onset of dementia would be extremely helpful in understanding the biological origins of AD and in designing appropriate interventions. Brain imaging provides a window into many of the hypothesized biochemical, functional and anatomic changes in AD. With positron emission tomography (PET) using [^{11}C]PIB it is possible to estimate the density of beta-amyloid ($\text{A}\beta$) plaques by imaging the PIB binding sites. With [^{18}F]FDG PET it is possible to estimate neuronal function from measures of metabolic activity. Finally, with magnetic resonance imaging (MRI) loss of brain tissue over time can be quantified in regional and global brain volume measures. It is our premise that by examining the temporal and spatial interrelationships between these three measures important insights will be gained into the pathophysiology of AD. The value of the imaging measures is further amplified when combined with the complimentary data of CSF biomarkers and clinical and psychometric evaluations.

PET:

Sites collecting PET scans must use a PET scanner that has been qualified to scan DIAN subjects. After images are uploaded into the Central Neuroimaging Database Archive (CNDA), quality control will be done by the Imaging Core team at the University of Michigan (headed by Dr. Robert Koeppe) and processing will be done by the Imaging Core team at Washington University (headed by Dr. Tammie Benzinger).

Scan Acquisition: Participant preparation consists of intravenous catheterization followed by the bolus injection (over 10-60 sec) of PIB (minimum 8 mCi, maximum 18 mCi). There are two acceptable procedures for obtaining the PIB PET scans. In one approach, the subject will rest quietly for approximately 30 minutes after injection and then be positioned in the scanner for scanning which will start 40 minutes after injection. In the second approach the subject will be positioned in the scanner at the time of injection and a 70 minute scan will be obtained starting at the time of injection. The first approach consists of the minimum dataset needed for analysis, while the second approach will allow more complex data analysis and modeling of the kinetic properties of the tracer. The site PI will have complete flexibility as to which approach to use for each PET PIB scanning session.

Specifically, in the first approach the PET scan will be acquired in dynamic, 3D imaging mode for 30 min (consisting of 6 x 5 min frames) beginning 40 min (+/- 30 seconds) after injection of PIB. In the second approach PET scan will be acquired in dynamic, 3D imaging mode for 70 min (consisting of 4 x 15 sec frames, 8 x 30 sec frames, 9 x 60 sec frames, 2 x 180 sec frames, 10 x 300 sec frames) beginning at the time of injection. No blood sampling will be performed for the PIB PET study. A standard brain transmission scan (or CT transmission scan for PET/CT scanners) will be obtained for attenuation correction after the emission data acquisition, or prior to acquisition if obtaining a CT transmission. Subjects will be removed from the scanner following the completion of the transmission scan (See PET Protocol below).

PET FDG:

Scan Acquisition: Subjects to receive a PET FDG scan in the morning are asked to omit all food and fluids (except water) from midnight the night before the FDG scan (or FDG and PIB if done on the same day) 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 FDG injection. Upon arrival to the imaging center, compliance to the dietary requirements should be confirmed and blood glucose level should be checked. Blood glucose level should be < 140 mg/dL (7.8 mmol/L). If BGL \geq 140 mg/dL, rescheduling the subject should be considered. If this is not an option, the scan should continue and a note should be made on the metadata form in the appropriate comment box following the

blood glucose record.

Typically, the PIB scans will be followed closely by the FDG scans on the same day; however, this arrangement is for convenience to the subject and coordinators but is not a requirement (see Appendix A for schema). After completion of PIB scanning, subjects will be moved to a dimly lighted, quiet room and 5 ± 0.5 mCi of FDG will be injected as a bolus. About 20 min later, subjects will be repositioned in the PET scanner, and FDG PET scans will be acquired in dynamic, 3D mode beginning 30 min (+/- 30 seconds) after injection of FDG for 30 min (consisting of 6 x 5 min frames). A standard brain transmission scan (or CT transmission scan for PET/CT scanners) will be obtained for attenuation correction after the emission data acquisition, or prior to acquisition if obtaining a CT transmission. (The transmission scan for the PIB scan cannot be used for the PET FDG scan.) Subjects will be removed from the scanner following the completion of the transmission scan.

Note: The injection of the FDG should be timed so that a minimum of 120 minutes (about 6 half-lives of C-11) will elapse from the time of injection of PIB to the start of the FDG scan. This means that a minimum of 90 minutes should elapse between the time of injection of PIB and the time of injection of FDG to provide for the nearly complete decay of C-11. Subjects may drink water (in moderation) between the PIB and FDG scans, but no food intake will be permitted (in compliance with the recommended 4 hour fast prior to the FDG scan).

General Information

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

This manual contains information for study-site staff involved with the care of the study participants during the imaging procedures and those involved with scanning the study participants.

Contact Information

If you have any questions or concerns regarding PIB or FDG PET imaging study please contact:

DIAN-PET@dian-info.org

If you have question regarding the scan uploading to the CNDA please contact:

cnda-help@dian-info.org

Site Qualification

Your institution must obtain separate human research approvals that specifically include the use of radioactive tracers prior to enrolling participants for the PIB protocol.

Scanner qualification:

All PET performance sites will be required to obtain scanner qualification by the University of Michigan team and Robert Koeppe, PhD (koeppe@umich.edu) before conducting scans. This procedure will require the scanning of a radioactive (<1 mCi 18F activity) Hoffman 3-D brain phantom on two separate days using the specified DIAN PET protocol. This phantom will be provided, on a temporary basis, to the performance site by the DIAN Imaging Core. The PET protocol will be provided to the performance site and will be specific to the PET scanner make and model. Subsequently, the acquisition and reconstruction parameters for the human subjects must be the same as used in the phantom scanning (with specific scans for both the human PIB and FDG PET acquisitions). Reconstructed resolution will be using the equivalent of a ramp filter (i.e., near the intrinsic resolution of the scanner) as this allows maximum flexibility during processing and analysis. Scanner specific qualifications will come from Dr. Robert Koeppe.

After acquisition and reconstruction, phantom image data will be uploaded to the Central Neuroimaging Data Archive (CNDA), retrieved by the University of Michigan team, and reviewed. If problems are identified with the phantom scans, the site will be contacted directly by Dr. Koeppe's team, the relevant issues will be discussed, and specific changes suggested. Qualification scans and review will be repeated (and iterated) until the site is qualified. Once the site is qualified the Hoffman 3-D brain phantom is then returned to the Imaging Core as directed by the University of Michigan team.

PIB [¹¹C]2-(4'-methylamino-phenyl)-6-hydroxy-benzothiazole qualification) Prior to conducting PET PIB studies, each site will be qualified by Chet Mathis, PhD., (mathisca@upmc.edu) at the University of Pittsburgh, for PIB production. If the site is not yet producing PIB for human use, Dr. Mathis will provide preclinical toxicology,

evidence for lack of human pharmacologic actions, and a sample PIB Drug Master File (DMF). It is expected that each site will need to adapt the DMF to their local environment. Dr. Mathis will be available for consultation during this phase.

Once your institution has received human research approvals that specifically include the use of radioactive tracers approval, AND your site has passed the phantom QC imaging, your site is ready to scan DIAN subjects. If your site is doing PIB, production approval must also be obtained before scanning DIAN subjects, see above.

Continued Quality Monitoring During Execution Phase

All MRI, PET PIB and PET FDG image data sets uploaded from any site will be quarantined in the Central Neuroimaging Data Archive (CNDA) until the data is passed by the appropriate image QC team. As described above all review of images should occur within two working days and the performance site will be contacted if a study does not meet criteria.

PET Pre-Scan Procedures / General Information

Participant Pre-screening

All participants should have been screened by the study coordinator for the following contraindications:

- Inability to cooperate/claustrophobia (sedation is not offered for this protocol)
- Inability to lie on the scanner bed for two 30-70 minute scan sessions for PIB and FDG imaging.
- Inability to achieve venous access sufficient for tracer administration

Subject Preparation

Subjects to be imaged in the morning are asked to omit all food and fluids (except water) from midnight the night before the FDG scan (or FDG and PIB if done on the same day) 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 FDG injection.

Image Subject/Session Identification

The subject ID will be generated by the Alzheimer's Disease Cooperative Study and assigned by the Clinical Study Coordinator at the clinical site prior to the PET visit. These IDs will be seven digit numbers (e.g. 9000001). Session identifiers, which distinguish between a subject's visits, will be provided by the CNDA. These IDs will be a composite of the subject ID, the visit number (e.g. v00, v01, v02) and the acquisition type (e.g. 9000001_v00_FDG, 9000001_v00_PIB). Each PET scan session will have a separate ID independent of whether they are obtained on the same day or not. For phantom scans, a subject representing the phantom may have to be created in the database if the phantom has not been scanned previously. Please see Appendix B for instructions on creating a phantom subject. The ID for the phantom subject will look like DIAN_{Site ID}_P (e.g. DIAN_007_P) and the session ID for phantom acquisitions will look like DIAN_{Site ID}_P_{Date of Scan} (e.g. DIAN_007_P_090101).

Entering Subject Information

If using a DICOM or ECAT scanner, please enter the subject's information into the scanner following your standard local practice. This will assure the scan is formatted for your local archival system. When data are uploaded to the CNDA, the scan header will be de-identified and rendered HIPAA compliant. Data will be identified in the CNDA by subject code only.

When you upload the data to the CNDA, you will be required to select the appropriate subject from a list of DIAN subjects already entered in the database.

Documentation

Be sure to complete the metadata sheet *as the study is being acquired*. The PET scan information form must be provided by the study coordinator prior to the scan.

IMPORTANT: There is a different metadata sheet specifically for PIB PET imaging and one for FDG PET imaging. Regardless of whether both PIB and FDG imaging are being conducted in the same imaging session, both forms need to be completed for all studies.

Sample PIB Metadata Forms

DIAN

PIB Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial Follow-up___

Site Code:

Study Coordinator Name:

DIAN Participant Initials:

PET Technologist Initials:

NOTE: Every visit should have ORIGINAL scan data entered before any rescan data is entered

If the participant is a woman of childbearing potential, please report the following:

Has the participant had a negative urine pregnancy test in the last 7 days? Yes No

If there is a chance the participant could be pregnant, she should not continue with the study procedures.

If the participant is a lactating mother, is she aware of the guidelines regarding lactation and PIB? Yes No

If the participant is lactating, please refer her to the research coordinator for lactation guidelines.

Was the scan conducted?

Yes

No

Reason why the scan was not conducted:

Illness

Participant unavailable

Participant unwilling

Administrative problems

Withdrawn consent

Other (specify)

Comments:

DIAN

PIB Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up___

Please note that in the event that the scan is not completed but the transmission or CT was acquired, please contact cnda-help@dian-info.org for further assistance.

Scan Date

Month	Day	Year
<input type="text"/>	<input type="text"/>	<input type="text"/>

If you are not using the scanner you were qualified for, please contact Dr. Koeppe, koeppe@umich.edu, for prior approval and explain below.

Time of today's Scanner QC

Enter '00' for seconds portion of the time if seconds are unavailable.

 HH:MM:SS

Time of PIB dose assay

Enter '00' for seconds portion of the time if seconds are unavailable.

 HH:MM:SS

PIB dose assay to nearest 0.1 mCi

 mCi

Time of residual PIB assay

Enter '00' for seconds portion of the time if seconds are unavailable.

 HH:MM:SS

Residual left in syringe if >0.1 mCi

 mCi

Net injected dose of PIB

corrected for residual activity to nearest 0.1 mCi

 mCi

PIB volume

 ml

DIAN

PIB Scan Information

Participant:

		/ /
--	--	-----

Participant ID

Session ID

Date of Scan

Visit: Initial; Follow-up___

Time of PIB injection

Enter '00' for seconds portion of time
if seconds are unavailable.

HH:MM:SS

Time scan started (emission)

Enter '00' for seconds portion of the time
if seconds are unavailable.

HH:MM:SS

Provide an explanation if start time varies from protocol:

SECTION II. SCAN PROTOCOL INFORMATION

Any variations from protocol during PIB uptake?

Yes

No

If Yes, describe:

Predefined acquisition protocol ID

Subject motion problems:

Yes

No

If yes, describe:

DIAN

PIB Scan Information

Participant:

		/ /
--	--	-----

Participant ID

Session ID

Date of Scan

Visit: Initial; Follow-up___

Scanner malfunction:

Yes

No

If yes, describe:

--

Other protocol variations:

Yes

No

If yes, describe:

--

SECTION III. SCAN RECONSTRUCTION

Check which of the following reconstructions was used:

FORE/2D-OSEM

OSEM3D-OP

3D-Ramla

3D Back-projection

If OSEM:

subsets:

14

16

N/A

Other

If Other, specify

--

iterations:

2

4

6

Other

DIAN

PIB Scan Information

Participant:

		/ /
--	--	-----

Participant ID

Session ID

Date of Scan

Visit: Initial; Follow-up___

If Other, specify:

If Ramla, Lambda=0.016?

Check here to confirm

If Back Projection, Ramp filter?

Check here to confirm

If FORE/2D-OSEM, Brain Mode "ON"

Check here to confirm

Check here if using scanner without Brain Mode

No post-process smoothing:

Check here to confirm

Decay Correction

Yes

No

If using a CT for attenuation, verify effective mAs is between 23-50 mAs

 mAS

Scatter Correction:

Yes

No

Attenuation Correction:

CT

Ge-68+Segmentation

Cs-137+Segmentation

DIAN

PIB Scan Information

Participant:

		/	/
--	--	---	---

Participant ID

Session ID

Date of Scan

Visit: Initial; Follow-up ___

SECTION IV. DATA TRANSFER AND ARCHIVE:

Was data transferred to CNDA within 24 hours of scan?

Data must be transmitted to CNDA within 24 hours of the PET scan. If your site is unable to complete the transfer within 24 hours please indicate the problem in the "Comments" section below.

- Yes
- No

Transfer Date

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Month	Day	Year					

Comments:

--

Data Archived Locally

If No, please explain under comments.

- Yes
- No

Archive Medium

Comments

--	--

Sample FDG Metadata Forms

DIAN

FDG Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up ___

Site Code:

Study Coordinator Name:

DIAN Participant Initials:

PET Technologist Initials:

NOTE: Every visit should have ORIGINAL scan data entered before any rescan data is entered.

If the participant is a woman of childbearing potential, please report the following:

Has the participant had a negative urine pregnancy test in the last 7 days? Yes No

If there is a chance the participant could be pregnant, she should not continue with the study procedures.

If the participant is a lactating mother, is she aware of the guidelines regarding lactation and FDG? Yes No

If the participant is lactating, please refer her to the research coordinator for lactation guidelines.

Was the scan conducted?

Yes

No

Reason why the scan was not conducted:

- Illness
- Participant unavailable
- Participant unwilling
- Administrative problems
- Withdrawn consent
- Other (specify)

Comment:

--

Please note that in the event that the scan is not completed but the transmission or CT was acquired, please contact cnda-help@dian-info.org for further assistance.

DIAN

FDG Scan Information

Participant:

		/	/	
Participant ID	Session ID	Date of Scan		

Visit: Initial; Follow-up____

Scan Date

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Month	Day	Year					

If you are not using the scanner you were qualified for, please contact Dr. Koeppe, koeppe@umich.edu, for prior approval and explain below.

Time of today's Scanner QC

Enter '00' for seconds portion of the time if seconds are unavailable.

	HH:MM:SS
--	-----------------

Time of blood glucose measurement

Enter '00' for seconds portion of the time if seconds are unavailable.

	HH:MM:SS
--	-----------------

Blood Glucose (pre-FDG)

Proper Range: <140 mg/dL (If the BGL ≥140 mg/dL please consider rescheduling the subject. If this is not an option, continue with the data acquisition and provide explanation below.)

	mg/dL or mmol/L
--	------------------------

Time of FDG dose assay

Enter '00' for seconds portion of the time if seconds are unavailable.

	HH:MM:SS
--	-----------------

DIAN

FDG Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up___

FDG dose assay
to the nearest 0.1 mCi

mCi

Net injected dose of FDG
Corrected for residual activity
Proper Range: 4.5-5.5 mCi

mCi

FDG Volume
 ml

Time of FDG injection
Enter '00' for seconds portion of the time
if seconds are unavailable.

HH:MM:SS

Provide an explanation if blood glucose was measured after the FDG injection

Time of residual FDG assay
Enter '00' for seconds portion of the time
if seconds are unavailable.

HH:MM:SS

Residual left in syringe
if >0.1 mCi

mCi

DIAN

FDG Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up___

Time scan started (emission)

*Enter '00' for seconds portion of the time
if seconds are unavailable.*

	HH:MM:SS
--	-----------------

Provide an explanation if start time varies from protocol:

--

SECTION II. SCAN PROTOCOL INFORMATION

Any variations from protocol during FDG uptake?

- Yes
- No

If Yes, describe:

--

Predefined acquisition protocol ID

--

Subject motion problems:

- Yes
- No

If yes, describe:

--

DIAN

FDG Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up___

Scanner malfunction

Yes

No

If yes, describe:

Other protocol variations:

Yes

No

If yes, describe:

SECTION III. SCAN RECONSTRUCTION

Check which of the following reconstructions was used:

FORE/2D-OSEM

OSEM3D-OP

3D-Ramla

3D Back-projection

If OSEM:

subsets:

14

16

N/A

Other

If Other, specify

iterations:

2

4

6

Other

DIAN

FDG Scan Information

Participant:

		/ /
Participant ID	Session ID	Date of Scan

Visit: Initial; Follow-up___

If Other, specify:

If Ramla, Lambda=0.016?

Check here to confirm

If Back Projection, Ramp filter?

Check here to confirm

If FORE/2D-OSEM, Brain Mode "ON"

Check here to confirm

Check here if using scanner without Brain Mode

If using a CT for attenuation, verify effective mAs is between 23-50 mAs

mAs

No post-process smoothing:

Check here to confirm

Decay Correction

Yes

No

Scatter Correction:

Yes

No

Attenuation Correction:

CT

Ge-68+Segmentation

Cs-137+Segmentation

SECTION V. DATA TRANSFER AND ARCHIVE:

Was data transferred to CNDA within 24 hours of scan?

Data must be transmitted to CNDA within 24 hours of the PET scan. If your site is unable to complete the transfer within 24 hours please indicate the problem in the "Comments" section below.

Yes

No

DIAN

FDG Scan Information

Participant:

		/	/
Participant ID	Session ID	Date of Scan	

Visit: Initial; Follow-up___

Transfer Date

<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Month	Day	Year					

Comments

--

Data Archived Locally

If No, please explain under comments.

Yes

No

Archive Medium

Comments

--	--

Scanner Parameters and Reconstruction

Siemens HR+ scanner:

Scan: emission: Sites can choose between two PET protocols to be administered for PIB; one protocol is a 70 minute [(4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames] 3-D dynamic PIB acquisition scan starting at the time of injection and the other is a 40 minute uptake followed by a 30 minute (6 x 300 sec frames) 3-D dynamic PIB acquisition. The FDG protocol will be acquired as a 30 minute uptake followed by a dynamic 3-D acquisition for 30 min, acquired as 6 x 300 sec frames. See Appendix A.

(The below parameters will be used for both the PIB and the FDG Human protocols).

Record: prompts and randoms rates at the start of acquisition.

Scan: transmission: 5 min 2-D scan post-emission scan. Process with segmentation and re-projection.

Reconstruction: FORE followed by 2D-OSEM, 4 iterations, 16 subsets, no smoothing, zoom=2.0. Reconstruct into 128x128 grid. Brain mode must be set to "ON".

Siemens BioGraph PET/CT scanner:

Scan: transmission: CT scan

Scan emission: Sites can choose between two PET protocols to be administered for PIB; one protocol is a 70 minute [(4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames] list-mode 3-D dynamic PIB acquisition scan and the other is a 40 minute uptake followed by a 30 minute (6 x 300 sec frame) list-mode 3-D dynamic PIB acquisition. The FDG protocol will be acquired as a 30 minute uptake followed by a list-mode 3-D acquisition for 30 min, binned as 6 x 300 sec frames.

(The below parameters will be used for both the PIB and the FDG Human protocols).

Record: prompts and randoms rates at the start of acquisition (if this is still possible, otherwise get prompts and randoms from scan headers).

Reconstruction: FORE followed by 2D-OSEM, 4 iterations, either 14 or 16 subsets (depending on the software version), no smoothing. Reconstruct into 336x336 grid if software no longer allows "TRIM" to be used. For software still allowing "TRIM", reconstruction into a 168x168 grid is okay.

The button saying "Match CT slices" needs to be turned OFF. With this button on, PET gets interpolated onto the CT slice spacing. Clicking this button off allows the PET data not being interpolated and results in either 81 or 109 PET slices for the standard 3-ring and extended FOV 4-ring (TrueV) systems, respectively.

GE Discovery PET/CT scanners:

Scan: transmission: CT scan

Scan emission: Sites can choose between two PET protocols to be administered for PIB; one protocol is a 70 minute [(4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames] 3-D dynamic PIB acquisition scan and the other is a 40 minute uptake followed by a 30 minute (6 x 300 sec frames) 3-D dynamic PIB acquisition. The FDG protocol will be acquired as a 30 minute uptake followed by a dynamic 3-D acquisition for 30 min, acquired as 6 x 300 sec frames. See Appendix A.

(The below parameters will be used for both the PIB and the FDG Human protocols).

Record: prompts and randoms rates at the start of acquisition (if this is not possible, get prompts and randoms from scan headers).

Reconstruction: Two reconstructions are needed. 1.) 3D-backprojection (reprojection) with ramp filter, and 2. OSEM reconstruction: 4 iterations 16 subjects with no smoothing. Ramp filters will vary depending on the model (and possible software version). Headers should say the following:

Disc LS: Rad:\rectangle\4.000000 mm\Ax:\rectangle\8.500000 mm

Disc ST: Rad:\rectangle\6.300000 mm\Ax:\rectangle\6.500000 mm or
Rad:\rectangle\6.400000 mm\Ax:\rectangle\6.500000 mm

Disc STE: Rad:\rectangle\4.800000 mm\Ax:\rectangle\6.500000 mm

Questions:

Contact: Bob Koeppe (Koeppe@umich.edu)

IMPORTANT: There are two acceptable approaches for collecting the PIB PET imaging.

Depending on scanner availability and subject tolerance, sites can chose between two PET protocols to be administered; one protocol is a 70 minute [(4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames] dynamic PIB acquisition scan and the other is a 40 minute uptake followed by a 6 x 300 sec frame dynamic PIB acquisition, also detailed in Appendix A. Please be sure to create separate acquisition protocols for PIB and FDG to ensure proper labeling.

IMPORTANT: For all sites with PET-only scanners, post-emission transmission scans should be collected for the DIAN FDG and PIB protocols.

Please note that if your site is collecting dynamic PIB with 33 frames, the patient should be marked prior to the start of the scan and realigned prior to the start of the frame at 40 minutes post-injection. This will help to reduce motion problems.

6 x 300 sec Frame Dynamic PIB Acquisition / Standard 6 x 300 sec Frame Dynamic FDG Acquisition.

- Upon arrival to the imaging center, compliance to the dietary requirements should be confirmed. Have the patient use the restroom and empty their bladder.
- Allow them to lie comfortably in a bed or reclining chair in a room in which the ambient noise is minimal and the degree of lighting can be controlled and minimized. Supply them with blankets/pillows as needed to maximize their comfort.
- Obtain intravenous access using either a small butterfly needle or angiocath. At this time blood glucose level should be checked. Optimally, blood glucose level should be <140 mg/dL (7.8 mmol/L). If BGL is \geq 140 mg/dL, consider rescheduling the patient if possible. If this is not an option, please provide an explanation on the metadata form in the appropriate comment box following the blood glucose record.
- Draw PIB (minimum 8 mCi, maximum 18 mCi) and assay with a dose calibrator. **Record the assayed dose (to the nearest 0.1 mCi) and assay time to the nearest minute. In the event of difficulties with radiochemical yields, the scan should not be performed if <8 mCi are available for injection. In this case the scan should be rescheduled.**
- Inject the PIB over 10-60 seconds. Rinse the syringe and flush the line with at least 10 cc of normal saline. **Record the injection time to the nearest minute. Do NOT discontinue the IV line at this time as it will be used for the FDG scan as well, if FDG is being done on the same day.**
- Re-assay the dose syringe and record the residual activity and time of assay. Allow the subject to rest comfortably in the room for 30 minutes for the incorporation of PIB into the brain.
- At the end of the 30 minute incorporation period, have the patient use the restroom and empty their bladder. (*Note* Depending on subject capabilities, this process may need to start prior to 30min to ensure the scan begins in a timely manner.)
- Position and secure the subject in the scanner using appropriate head restraints.
- Acquire a **dynamic**, 3D scan consisting of 6 x 300 sec frames beginning 40 minutes +/- 30 seconds after tracer injection. Obtain post emission attenuation, unless using a PET/CT.
- *Upon completion the subject can be removed from the scanner and encouraged to void. The patient will have a break of approximately 10 minutes before the FDG study can begin. This is to permit adequate decay of PIB from the brain (90 min, see below, from the time of PIB injection to the start time of the FDG PET injection.)
- Subjects may drink water (in moderation) between the PIB and FDG scans, but no food intake will be permitted (in compliance with the recommended 4 hour fast prior to the FDG scan).
- After completion of PIB scanning, subjects will be moved to a dimly lighted, quiet room and 5 \pm 0.5 mCi of FDG will be injected as a bolus. **Record the assayed dose and assay time to the nearest minute.**
- Rinse the syringe and flush the line with at least 10 cc of normal saline. **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 for 20 minutes for the incorporation of FDG into the brain. During the incorporation period, the patient's eyes should be open and the ears should remain un-occluded.
- At the end of the 20 minute incorporation period, have the patient use the restroom and empty their bladder. (*Note* Depending on subject capabilities, this process may need to start prior to 20min to ensure the scan begins in a timely manner.)

- Reposition the subject in the PET scanner. FDG PET scans will be acquired in dynamic, 3D mode beginning 30 min after injection of FDG for 30 min (6 x 5 min frames).
- A second transmission scan will be obtained for attenuation correction and subjects will be removed from the scanner following the completion of the second transmission scan. (*Note* If using a PET/CT scanner, the CT transmission will be done prior to the data acquisition.)
- Note: The injection of the FDG should be timed so that a minimum of 120 minutes (about 6 half-lives of C-11) will elapse from the time of injection of PIB to the start of the FDG scan. This means that a minimum of 90 minutes should elapse between the time of injection of PIB and the time of injection of FDG to provide for the nearly complete decay of C-11.

70 minute Extended Dynamic PIB Acquisition/Standard 6 x 300 sec Frame Dynamic FDG Acquisition.

- Upon arrival to the imaging center, compliance to the dietary requirements should be confirmed.
- Have the patient use the restroom and empty their bladder.
- Obtain intravenous access using either a small butterfly needle or angiocath. At this time, blood glucose level should be checked. Blood glucose level should be <140 mg/dL (7.8 mmol/L). If BGL is \geq 140 mg/dL, consider rescheduling the patient if possible. If this is not an option, please provide an explanation on the metadata form in the appropriate comment box following the blood glucose record.
- Position the subject in the scanner using appropriate head restraints.
- Draw PIB (minimum 8 mCi, maximum 18 mCi) and assay with a dose calibrator. ***Record the assayed dose (to the nearest 0.1 mCi) and assay time to the nearest minute. In the event of difficulties with radiochemical yields, the scan should not be performed if <8 mCi are available for injection. In this case the scan should be rescheduled.***
- Inject the PIB over 10-60 seconds. Rinse the syringe and flush the line with at least 10 cc of normal saline. ***Record the injection time to the nearest minute. Do NOT discontinue the IV line at this time as it will be used for the FDG scan as well, if FDG is being done on the same day.***
- Re-assay the dose syringe and record the residual activity and time of assay.
- Acquire a ***dynamic***, 3D scan consisting of the following:
 - 4 x 15 sec frames
 - 8 x 30 sec frames
 - 9 x 60 sec frames
 - 2 x 180 sec frames
 - 10 x 300 sec frames
 - Obtain post emission attenuation (unless using a PET/CT)

*Please see previous scanning protocol for FDG scanning instructions.

PET Only Scanners

Acquire an attenuation correction scan using rod sources for 5-6 minutes after the acquisition of the emission scan. Segmentation and re-projection routines will be applied for attenuation correction.

PET/CT Scanners

Standard CT acquisition parameters. Verify effective mAs is between 23-50 mAs.

Note Siemens Biograph scanners should have the “Match CT Slice” turned off.

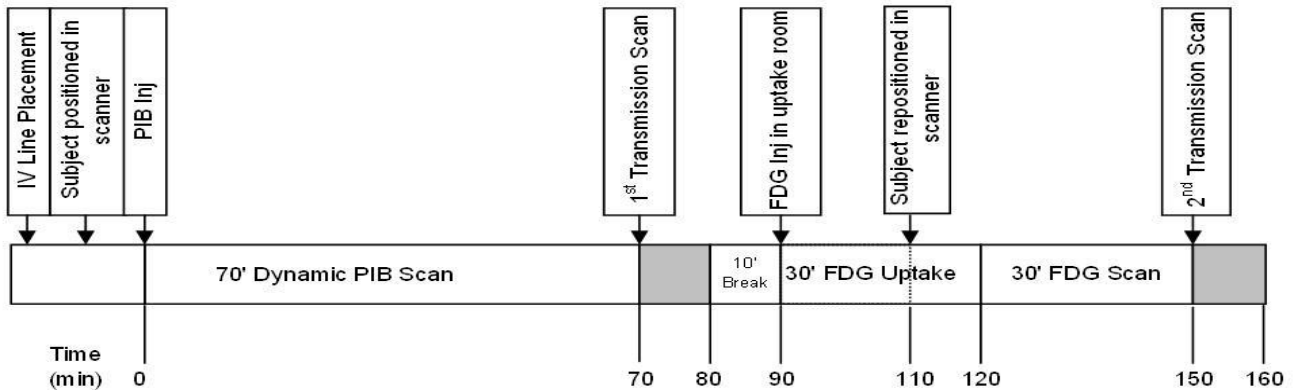
Typically, the PIB scans will be followed closely by the FDG scans on the same day; however, this is for convenience to the subject and coordinators but is not a requirement (see below for schemas).

Appendix A –Examples of PIB / FDG Protocols (*Note* the below schema do not account for use of a PET/CT scanner. CT transmissions will be obtained prior to emission data acquisitions.)

Example 1: 70 min Extended Dynamic PIB and Standard 6 x 300 sec Frame Dynamic FDG

Framing Sequence

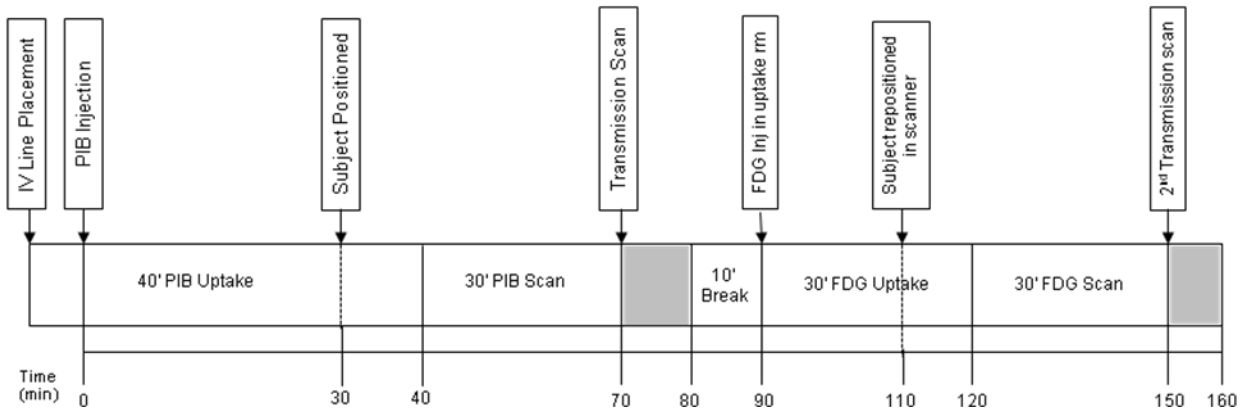
- PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames starting at time of PIB injection
- FDG: (6 x 300s) frames starting 30 min post FDG injection.



Example 2: 6 x 300 sec Dynamic PIB and Standard 6 x 300 sec Frame Dynamic FDG

Framing Sequence

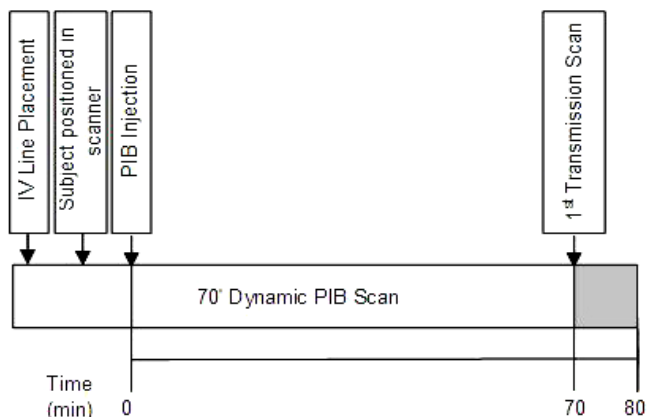
- PIB: (6 x 300s) frames starting 40 min post PIB injection
- FDG: (6 x 300s) frames starting 30 min post FDG injection



Example 3: 70 min Extended Dynamic PIB Only (Single Day)

Framing Sequence

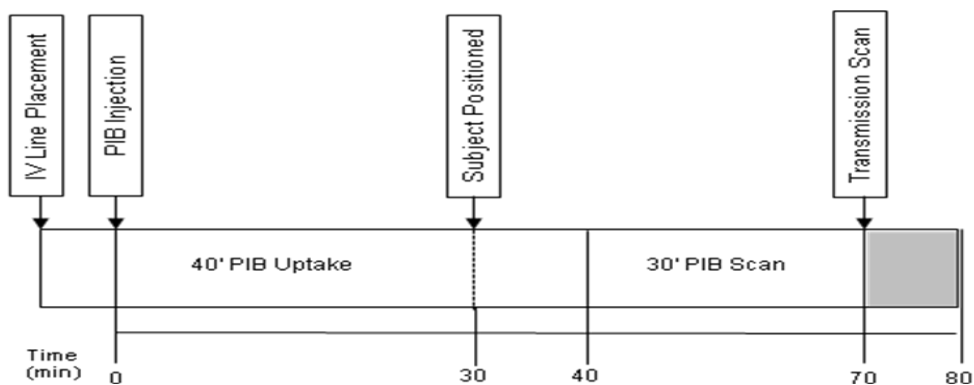
- **PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames starting at time of PIB injection**



Example 4: Standard 6 x 300 sec Dynamic Acquisition PIB Only (Single Day)

Framing Sequence

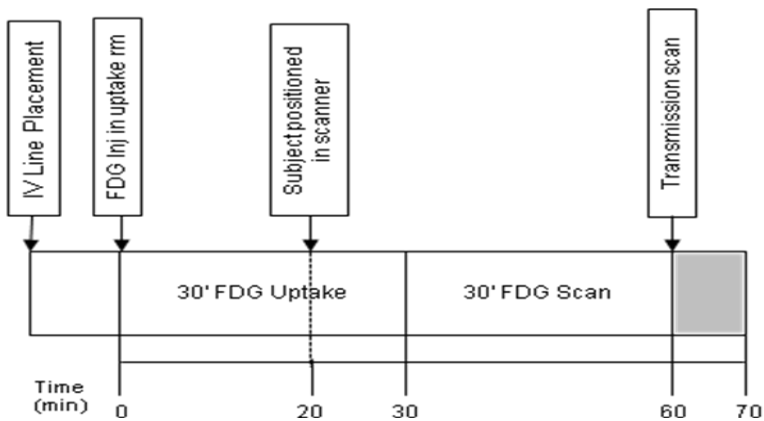
- **PIB: 6 x 300 second frames starting at 40 minutes post PIB injection**



Example 5: Standard 6 x 300 sec Frame Dynamic FDG (Single Day)

Framing Sequence

➤ **FDG: 6 x 300 second frames starting at 30 minutes post FDG injection**



Continuous Real Time Quality Control :

All MRI, PET PIB and PET FDG image data sets uploaded from any site will be quarantined in the CNDA until the data is passed by the appropriate image QC team. All review of images should occur within two working days and the performance site will be contacted if a study does not meet criteria.

After completion of the full QC procedures, a determination will be made as to whether the scan passes or fails. In the event of scans failing QC the Imaging Core will inquire with the performance site as to the suitability of returning the patient for rescanning or if appropriate, correcting the existing scan.

Protecting Confidentiality:

The raw image files (DICOM or ECAT format) will be received by the Informatics Core over secure, encrypted channels. Prior to upload, the header section of the files will be automatically edited to remove identifying fields (e.g. participant name, date of birth). All image files distributed to the quality control sites and investigators will be labeled with the anonymous subject and study accession numbers generated by the ADCS and CNDA.