

**Alzheimer's Disease Neuroimaging Initiative
PET Technical Procedures Manual
Supplemental Imaging Protocol Using
Pittsburgh Compound B (PIB)**

**Version 1.2
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General Information

The purpose of this manual is to further explain the supplemental PET imaging component to assess the amyloid plaque burden using [C-11] Pittsburgh Compound B (PIB) in a subset of ADNI subjects that have also been randomized to FDG PET imaging. Standard procedures are needed to ensure consistency of data collection in this longitudinal study.

PIB PET scans will be conducted in these groups.

MCI Group (n=48)

Entering subjects with no previous FDG PET will be scanned at 0, 12, 24, 36 months
Subjects with baseline and 6 month FDG PET will be scanned at 12, 24 and 36 months

AD Group (n=24)

Entering subjects with no previous FDG PET will be scanned at 0, 12, 24 months
Subjects with baseline and 6 month FDG PET will be scanned at 12 and 24 months

Control Group (n=24)

Entering subjects with no previous FDG PET will be scanned at 0, 12, 24, 36 months
Subjects with baseline and 6 month FDG PET will be scanned at 12, 24 and 36 months

Contact Information

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

adnipet@adni.ucsd.edu

If you have any questions or concerns regarding individual participants please contact the study coordinator at your referral site.

If you have question regarding the scan uploading to the LONI website please contact

adni@loni.ucla.edu

Site Qualification

Your institution must obtain a separate IRB approval, Radiation Safety Committee (RSC) or Radioactive Drug Research Committee (RDRC) approval prior to enrolling patients for the PIB protocol. In some cases your RDRC may indicate the necessity for an IND. All regulatory documents must be submitted to Kristin Woods (klwoods@ucsd.edu) at the ADCS prior to enrolling subjects. No PIB slots will be released until all regulatory approval has been obtained.

Sites which have passed the initial certification for FDG by scanning a Hoffman 3D brain phantom may begin PIB PET provided they have obtained the additional IRB and RSC/RDRC approvals. There are no additional phantom scans which need to be performed unless there is a change or upgrade in the hardware/software of the imaging system.

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. The details for PET and PET/CT scanners and ancillary equipment are detailed in the PET Technologists Manual used for the FDG imaging.

PET Pre-Scan Procedures / General Information

Participants 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 30-40 minute scan sessions for PIB and FDG imaging. There will be a short break between the two imaging sessions.
- Inability to achieve venous access sufficient for tracer administration (and venous blood sampling for the dynamic FDG protocol).

IMPORTANT: It is preferred that the PIB and FDG PET scans are performed on the same day. If this is not possible, the two studies may be performed within 28 days of each other and should take place within 2 weeks of the in-clinic visit.

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 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.

Participant Positioning

Proper patient positioning is a key aspect of the successful completion of the PET exam. Guidelines for patient positioning are described in detail in the PET Technologist Manual used for FDG imaging.

Ambient Conditions

Although the PIB uptake into the brain is independent of the ambient conditions, the patient should be allowed to rest quietly in a controlled environment similar to the FDG study.

Image File Identification

File identification will be conducted in a manner identical to that used for FDG PET imaging. The file ID will be assigned by the Clinical Study Coordinator at the clinical site prior to the PET visit. The naming convention is SSS_C ##### where SSS is the three digit site ID, C is either S (subject) or P (phantom), and ##### is the unique four digit number assigned by the site. For example, 129_S_0012 is the 12th subject enrolled in ADNI across all sites, from Banner Good Samaritan.

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. 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.

An example of the PIB metadata sheet has also been included on pages 7-10 of this manual.

Sample PIB Metadata Form

ADNI - Execution Phase (ADNI)	
PIB Scan Information	
Participant:	<input type="text"/>
Visit: Baseline	Participant ID

Was the scan conducted?

Yes
 No

Reason why the scan was not conducted:

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

If Other, specify:

Scan Date:
Month Day Year

Technologist Initials:

Select one of the following scanner vendors and models:

GE
 check here

Siemens/CTI
 check here

Phillips
 check here

If GE, Scanner Model:
 Advance
 Discovery LS
 Discovery ST
 Discovery RX

If Siemens/CTI, Scanner Model:
 ACCEL
 Biograph
 Biograph BGO
 Biograph HRZ
 EXACT
 HR+
 HRRT

If Phillips, Scanner Model:
 Allegro
 Allegro-Neuro
 Gemini
 Gemini GLX
 Gemini-TF

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

Time of residual PIB 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

Residual left in syringe
if >0.1 mCi
 mCi

ADNI - Execution Phase (ADNI)

PIB Scan Information

Participant:
Participant ID

Visit: Baseline

Net injected dose of PIB
corrected for residual activity
to exceed 0.1 mCi

PIB volume
 ml

Time of PIB injection
*Enter '00' for seconds portion of the time if seconds are unavailable.
PIB injections should be at least 90 min before a qualitative FDO and at least 120 minutes before a quantitative FDO.*
 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 is not within the allowable window
(Target: +90 min). If Scan time is not within + 45-55 min from PIB injection time, please provide explanation.

SECTION II. SCAN PROTOCOL INFORMATION

Any variations from protocol during PIB uptake?

- Yes
- No

If Yes, describe:

Predefined acquisition protocol ID

Indicate whether scan was static or dynamic:

- Static (1 x 20 min)
- Standard Dynamic (4 x 5 min)
- Dynamic (specify)

If dynamic indicate framing sequence:

- | | | | | |
|-------------------|----------------------|-----------|----------------------|---------|
| 1. No. of Frames | <input type="text"/> | Duration: | <input type="text"/> | seconds |
| 2. No. of Frames: | <input type="text"/> | Duration: | <input type="text"/> | seconds |
| 3. No. of Frames: | <input type="text"/> | Duration: | <input type="text"/> | seconds |

ADNI - Execution Phase (ADNI)

PIB Scan Information

Participant:

Participant ID

Visit: Baseline

4. No. of Frames:

Duration:

seconds

5. No. of Frames:

Duration:

seconds

6. No. of Frames:

Duration:

seconds

7. No. of Frames:

Duration:

seconds

8. No. of Frames:

Duration:

seconds

9. No. of Frames:

Duration:

seconds

10. No. of Frames:

Duration:

seconds

Subject motion problems:

Yes

No

If yes, describe:

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/3D-OSEM

OSEM3D-OP

3D-Ramla

3D Back-projection

If OSEM or Ramla:

subsets:

14

16

N/A

Other

ADNI - Execution Phase (ADNI)

PIB Scan Information

Participant:

Participant ID

Visit: Baseline

If Other, specify

iterations:

- 2
- 4
- 6
- Other

If Other, specify:

If Ramla, Lambda=0.016?

- Check here to confirm

If Back Projection, Ramp filter?

- Check here to confirm

If FORE2D-OSEM, Brain Mode "ON" for PET only scanners or TRIM "ON" for PET/CT scanners?

- Check here to confirm

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 IV. DATA TRANSFER AND ARCHIVE:

Was data transferred to LONI within 24 hours of scan?

Data must be transmitted to LONI 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

<input type="text"/>	<input type="text"/>
----------------------	----------------------

PET Imaging Protocol

IMPORTANT: There are acceptable variations of the framing rate for PIB PET imaging. The following section details the basic PIB protocol. Additional protocols which detail potential variations are also detailed in Appendix A. *However, it is required that your framing rate include 4 x 300 sec frames from 50 – 70 minutes post PIB injection.* If your site would like to perform an imaging method not documented in this manual, please contact a member of the ADNI PET core prior to proceeding (adnipet@adni.ucsd.edu). Please also be sure to create separate acquisition protocols for PIB and FDG to ensure proper labeling.

Standard 4 x 300 sec frame dynamic PIB acquisition / Standard 5 x 300 sec frame dynamic FDG acquisition

- Upon arrival to the imaging center, compliance to the dietary requirements should be confirmed and the blood glucose level checked.
- 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 as previously described. Supply them with blankets/pillows as needed to maximize their comfort.
- Obtain intravenous access using either a small butterfly needle or angiocath. Obtain baseline blood glucose level if not already performed.
- Draw 15 ± 1.5 mCi (555 MBq) of PIB 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 <10 mCi are available for injection. In this case the scan should be rescheduled.*
- Inject the PIB over 10-20 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.*
- Re-assay the dose syringe and record the residual activity and time of assay.

Allow the subject to rest comfortably in the room for 40 minutes for the incorporation of PIB into the brain.

IMPORTANT: This should be timed such that the patient will be on the scanner at 50 minutes after injection, ready for acquisition to begin.

- At the end of the 40 minute incorporation period, have the patient use the restroom and empty their bladder.
- Position and secure the subject in the scanner using methods previously described in the PET Technologist Manual for FDG.
- Acquire a *dynamic*, 3D scan consisting of 4 - 300 sec frames beginning approximately 50 minutes after tracer injection.

IMPORTANT: Biograph PET/CT users should acquire a single 20 minute frame since dynamic scanning capability is not currently available.

- All images will need to be corrected using measured attenuation.
 - 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
- 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 from the time of PIB injection to the start time of the FDG PET acquisition). The patient should be instructed not to eat or drink anything except water during the break.

IMPORTANT: If your site is performing *dynamic (quantitative)* FDG imaging, the time from the PIB injection until the time of the FDG injection should be increased from 90 to 120 minutes.

- Prior to beginning the FDG study, 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/non-water drink, wait until 2 hours have elapsed from last ingestion.

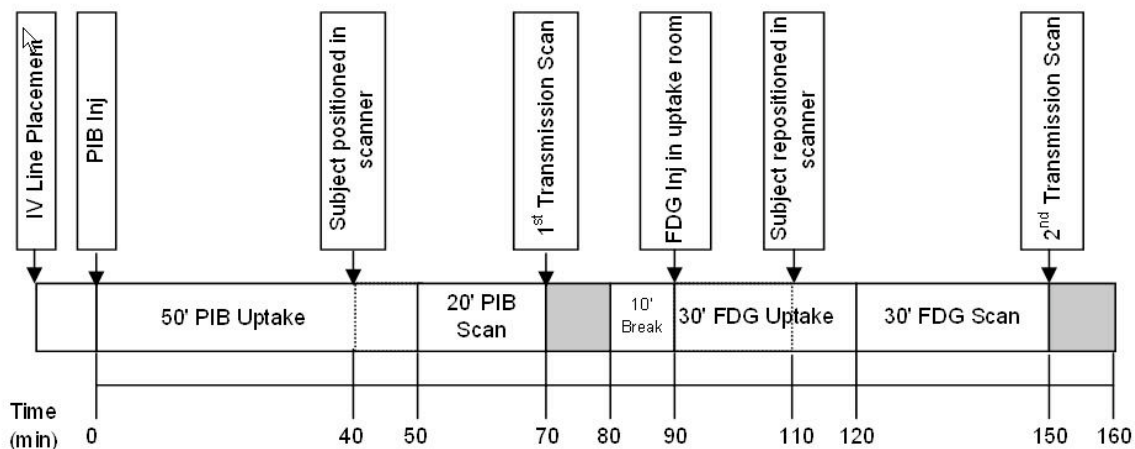
- Once >2 hour have elapsed since last ingestion, measure the blood glucose levels. If the blood glucose level is <180 mg/dL (9.9 mmol/L) then proceed with the scan. If not, the subject will need to wait an additional amount of time until the blood glucose levels meet the above criteria or reschedule.
- 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 as previously described. Supply them with blankets/pillows as needed to maximize their comfort.
- Verify the IV is patent and obtain baseline blood glucose level if not already performed.
- Draw 5 ± 0.5 mCi (185 MBq) of FDG and assay with a dose calibrator. **Record the assayed dose and assay time to the nearest minute.**
- Inject the FDG. 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.

IMPORTANT: This should be timed such that the patient will be on the scanner at 30 minutes after injection, ready for acquisition to begin.

- Position and secure the subject in the scanner using methods previously described.
- Acquire a *dynamic*, 3D scan consisting of 6 - 300 sec frames.

IMPORTANT: Biograph PET/CT users should acquire a single 30 minute frame since dynamic scanning capability is not currently available.

- All images will need to be corrected using measured attenuation.
 - 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
- Upon completion the subject can be removed from the scanner and encouraged to void. The subject should also be instructed to drink plenty of fluids and void frequently throughout the day to help reduce radiation exposure.
- Below is a schematic representation to assist with the timing constraints of the procedure.



- Reconstruct images using parameters specific to the system used for scanning. PIB and FDG data sets will be reconstructed with the same parameters. (See Appendix A in the PET Technologists Manual for details).
- Upon completion of the reconstruction, review all the images to assess for artifacts and motion.
- 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 ADNI project (approximately 5 years).

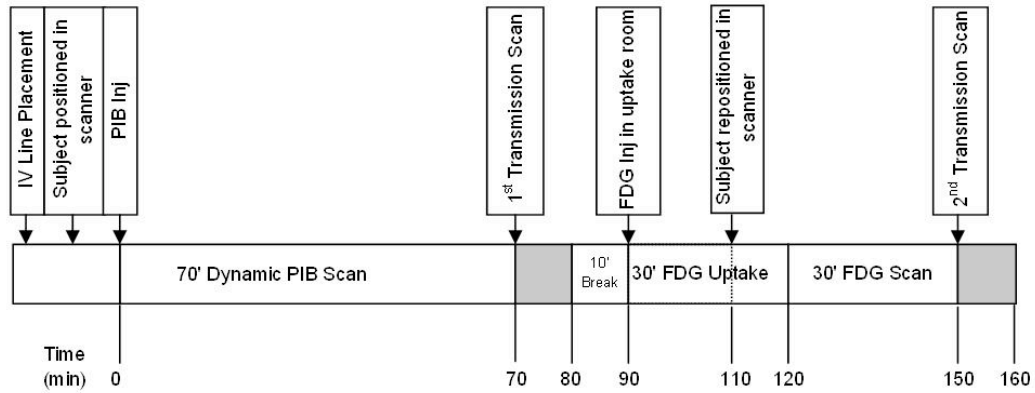
- Transfer both PIB and FDG image data to the Laboratory of Neuroimaging (LONI) at UCLA using the procedure detailed in Appendix B. These should be performed as separate uploads.

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.

Appendix A – Additional Examples of PIB / FDG Protocols

Example 1: 70 min Extended Dynamic PIB and Standard 5 x 300 sec frame dynamic FDG

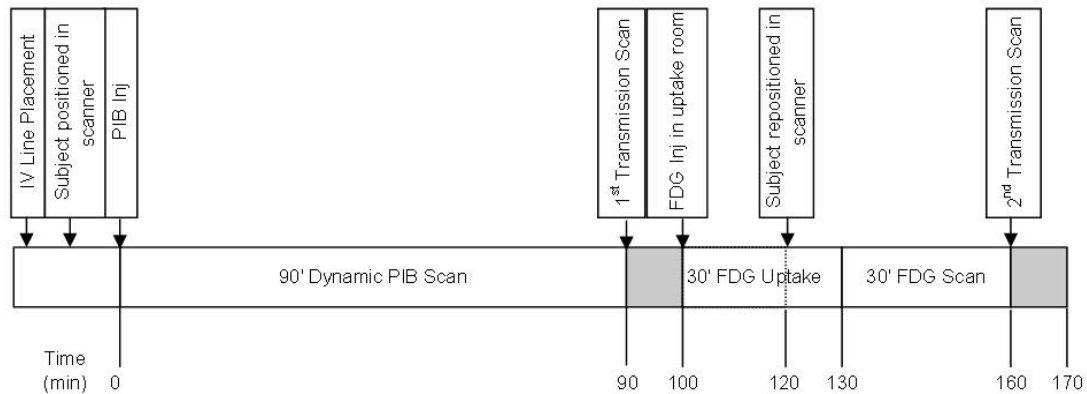
- PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames starting at time of PIB injection
- FDG: (5 x 300s) frames starting 30 min post FDG injection.



Example 2: 90 min Extended Dynamic PIB and Standard 5 x 300 sec frame dynamic FDG

Framing Sequence

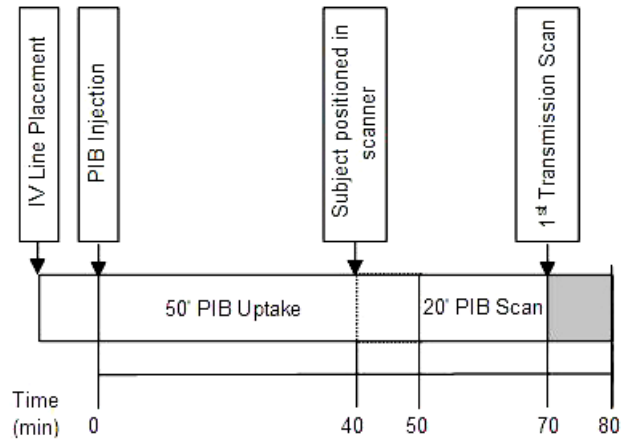
- PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(14 x 300s) frames starting at time of PIB injection
- FDG: (5 x 300s) frames starting 30 min post FDG injection.



Example 3: Standard 4 x 300 s dynamic acquisition PIB Only (Single Day)

Framing Sequence

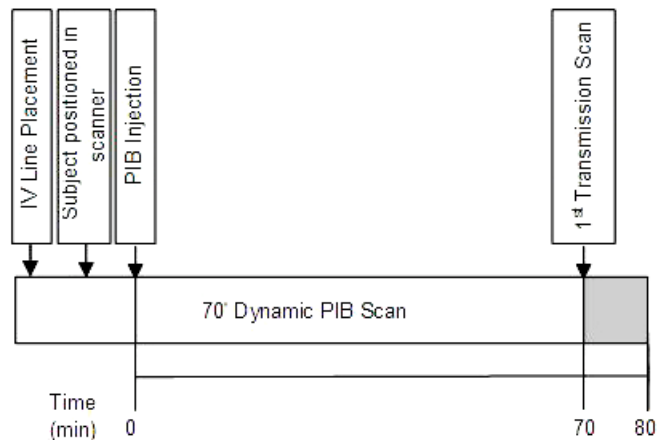
- **PIB: 4 x 300 second frames starting at 50 minutes post PIB injection**



Example 4: 70 min Extended Dynamic PIB Only (Single Day)

Framing Sequence

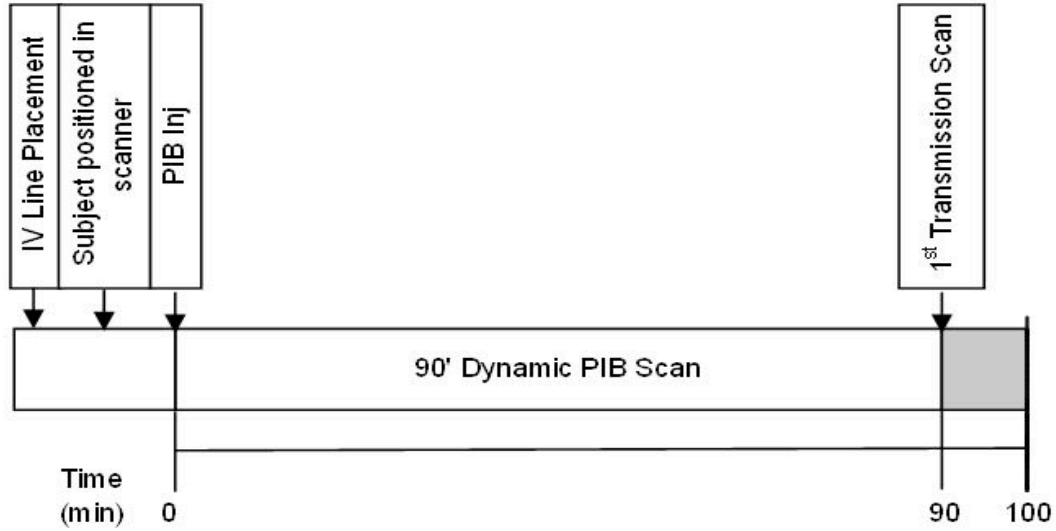
- **PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(10 x 300s) frames starting at time of PIB injection**



Example 5: 90 min Extended Dynamic PIB Only (Single Day)

Framing Sequence

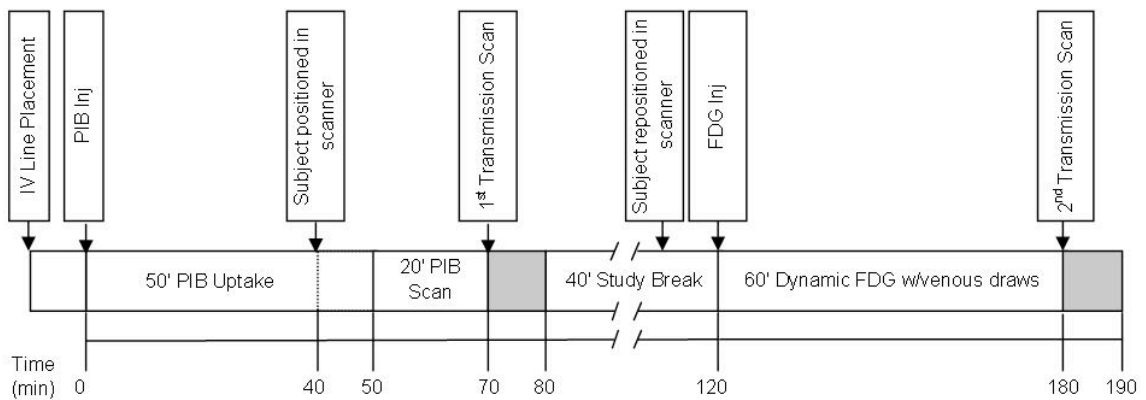
- PIB: (4 x 15s)(8x 30s)(9 x 60s)(2 x 180s)(14 x 300s) frames starting at time of PIB injection



Example 6: Standard 4 x 300 s acquisition PIB and Extended Dynamic (Quantitative) FDG (Note increased study break time = 40 min)

Framing Sequence

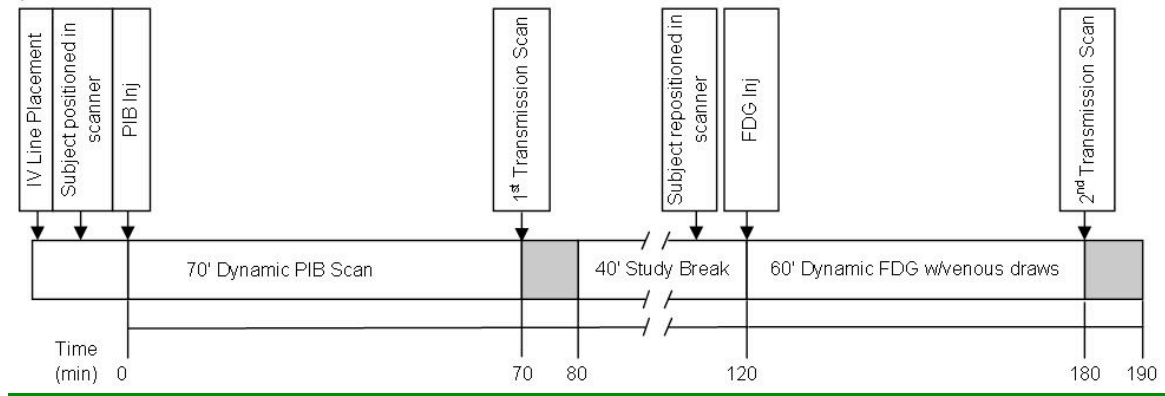
- PIB: 4 x 300 second frames starting at 50 minutes post PIB injection
- FDG: (1 x 10s)(12 x 5s)(2 x 10s)(3 x 30s)(3 x 60s)(2 x 120s)(10 x 300s) starting at time of FDG injection.



Example7: 70 min Extended Dynamic PIB and Extended Dynamic (Quantitative) FDG
(Note increased study break time = 40 min)

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: (1 x 10s)(12 x 5s)(2 x 10s)(3 x 30s)(3 x 60s)(2 x 120s)(10 x 300s) starting at time of FDG injection.**



Example8: 90 min Extended Dynamic PIB and Extended Dynamic (Quantitative) FDG
(Note increased study break time = 20 min)

Framing Sequence

- **PIB: (4 x 15s)(8 x 30s)(9 x 60s)(2 x 180s)(14 x 300s) frames starting at time of PIB injection**
- **FDG: (1 x 10s)(12 x 5s)(2 x 10s)(3 x 30s)(3 x 60s)(2 x 120s)(10 x 300s) starting at time of FDG injection.**

