BRIGHAM AND WOMEN'S HOSPITAL | Harvard Medical School

**Nuclear Reading Center | Brigham and Women's Hospital**


# Manual 35

# ARIC-PYP/HDP Procedures

## Version 2.1

## July 27, 2022

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**PYP/HDP SPECT Procedures**

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# 0 REVISIONS

| Version Number | Date | Author | Section(s) | Description of Update |
|---|---|---|---|---|
| 1.0 | Jan. 5, 2021 | Dorbala, Shah, Valint | All | Initial Draft for PYP Manual |
| 1.1 | Feb. 5, 2021 | Valint | Completing an Appointment (3.7) | Updated for Clarity. Updated based on Pilot Activity Responses. |
| 1.2 | Mar. 26, 2021 | Dorbala, Shah, Valint | Training and Certification (9), Data Transfer (7), and Appendix (13) | Updated Section 2, page 5, figure to add long term image storage at sites<br>Updated Section 9 to include brief description of ARIC field center staff training.<br>Update data transfer procedures to reflect correct methods. |
| 1.3 | Sep. 13, 2021 | Dorbala, Shah, Valint | Appendix (13) | Add the final PYP Summary of Results letter to the Appendix as Appendix VI. |
| 1.4 | Oct. 29, 2021 | Dorbala | Appendix (13) | Add suggested CPT codes for billing. |
| 1.5 | Jan 20, 2022 | Dorbala | Scheduling appointments<br>(3.3) | Removed the need to schedule PYP scans within 6 months of a study visit |
| 2.0 | March 9, 2022 | Dorbala | Adding Tc-99m-HDP (Oxidronate)<br>Excluding subjects with dementia/cognitive impairment when they are unable to consent<br>Removing consent by proxy | There is a shortage of Tc-99m-PYP in certain parts of the country. Therefore, we are adding Tc-99m-HDP as an alternate radiotracer for this study. Tc-99m-HDP is diagnostically equivalent with a similar safety profile and no difference imaging protocols.<br>Subjects who cannot consent for the study due to dementia or cognitive impairment will be excluded from the study. |
| 2.1 | July 27, 2022 | Dorbala, Nguyen | Appendix (13) | Clarified participant position exclusion for image preparation.<br>Edited study staff. |

# 1 LIST OF ABBREVIATIONS

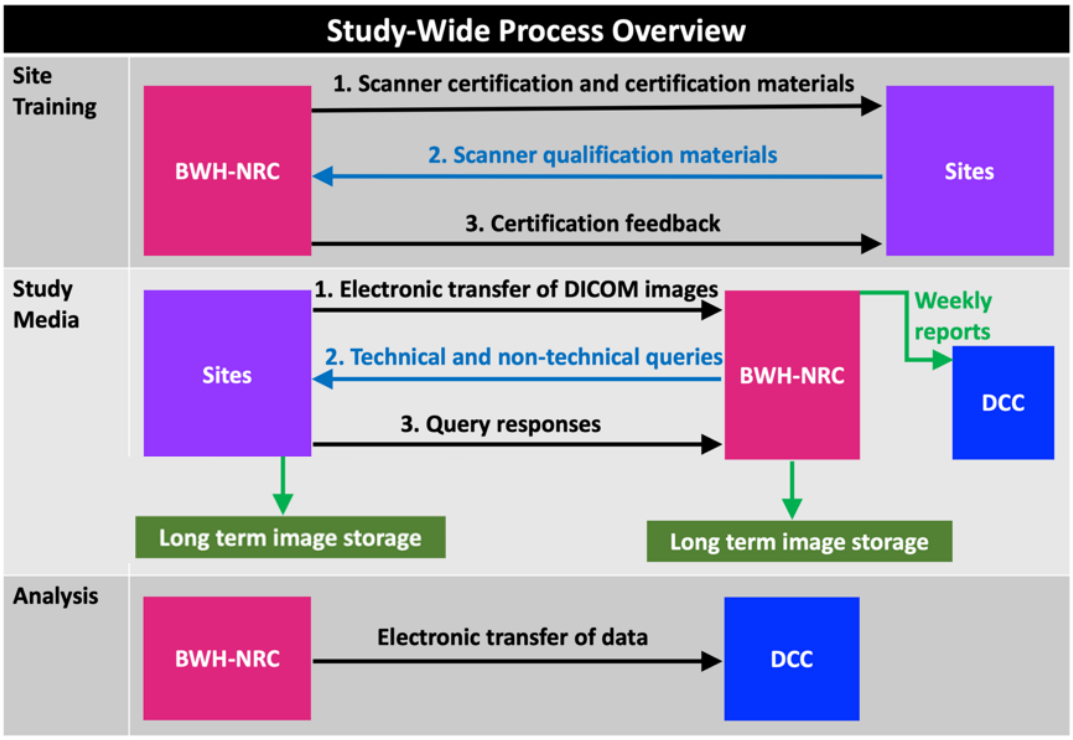
| | |
|---|---|
| ARIC | Atherosclerosis Risk in Communities |
| ATTR | Transthyretin |
| BWH-NRC | BWH Nuclear Reading Center |
| CA | Cardiac Amyloidosis |
| CDART | Carolina Data Acquisition and Reporting Tool |
| CT | Computed Tomography |
| DCC | Data coordinating center |
| HDP | Hydroxymethylene Diphosphonate (Oxidronate) |
| HF | Heart Failure |
| HFpEF | Heart Failure with Preserved Ejection Fraction |
| IRB | Institutional Review Board |
| LV | Left Ventricular |
| MACE | Major Adverse Cardiac Events |
| NCS | Neurocognitive Study |
| PACS | Picture Archiving and Communication System |
| PEX | Physical Exam form |
| PYP | Pyrophosphate |
| PYCD | PYP Clinical Data form |
| PYPC | PYP Procedure Completion form |
| PYRE | PYP Recruitment and Eligibility form |
| QxQ | Question by Question |
| RSX | Respiratory Questionnaire |
| SPECT | Single-Photon Emission Computed Tomography |
| Tc | Technetium |

# 2 OVERVIEW

Myocardial deposition of ATTR — transthyretin cardiac amyloidosis (ATTR-CA) — increases with age and is responsible for 13-18% of heart failure with preserved ejection fraction (HFpEF) in late life. ATTR-CA is particularly deadly with a 2-year mortality rate of 34% to 42% (Castano, Drachman, Judge, & Maurer, 2015; Cornwell 3rd, Westermark, Murdoch, & Pitkanen, 1982). Unfortunately, the diagnosis of ATTR-CA is often delayed by 1-2 years and until recently no specific therapies were available. This study, entitled *The Early Detection of Transthyretin Cardiac Amyloidosis: Defining a Novel Target for HFpEF Treatment and Prevention in Late Life*, is designed to harness recent breakthroughs in ATTR-CA diagnosis and therapy to treat and prevent this particularly malignant cause of HFpEF.

This manual of operations provides an overview of procedures for the $^{99m}$technetium pyrophosphate/Oxidronate imaging, that will be conducted within the Atherosclerosis Risk in Communities (ARIC) cohort. Procedures are performed utilizing standardized protocols. These protocols will be identical across participants. All personnel must be fully familiar with this manual of procedures, be trained and certified in the appropriate protocols, and remain consistent throughout data collection. Mastery of the procedures described in this manual is required so that patterns in the ARIC data can reflect differences between participants and their characteristics as opposed to differences between study technicians or field centers.

Field centers will electronically transmit PYP/HDP scan data directly to the Cardiovascular Imaging Core Laboratory Nuclear Reading Center (NRC) at the Brigham and Women's Hospital (BWH). Below is a diagram that depicts this process.




BWH-NRC – Brigham and Women's Hospital Nuclear Reading Center, DCC - Data coordinating center. Weekly reports sent to DCC by BWH research coordinator.

# 3 RECRUITMENT AND ASSESSMENT SEQUENCE

Most ARIC participants who enroll in the ARIC PYP Study will have 5 key interactions with project staff. A typical sequence is depicted below.

1. Participant receives a brochure for the study by mail or in-person during an ARIC visit.
2. Staff describe the study, gauge interest, and determine eligibility over the phone or in-person during an ARIC Visit. If the participant agrees to take part in the study, an appointment for a PYP/HDP scan will be scheduled.
3. Participant receives an appointment reminder letter, appointment location map, and a copy of the consent form approximately 5 to 7 days before the scheduled PYP/HDP scan.
4. Participant receives a reminder call approximately 2 days before the PYP/HDP scan.
5. Participant arrives for the appointment, signs the consent form, and completes the PYP/HDP scan along with a series of related tests including questionnaires focused on amyloidosis-related history and dyspnea.

The steps involved with each of these interactions are described below.

## 3.1 IDENTIFICATION OF POTENTIAL PARTICIPANTS

To be eligible for the PYP study, participants need to have a Visit 7 (or Visit 5 if Visit 7 is not available) echocardiogram showing LVEF >50% AND at least one of the following:

1. Have a history of heart failure
2. Have a left ventricular wall thickness greater than 12 mm in their most recent echocardiogram.
3. Have an amyloidogenic mutation (Val 122 I TTR gene mutation)
4. Have a longitudinal base-to-apex strain gradient greater than 1 in their most recent echocardiogram
5. Have at least one ARIC criteria for diastolic dysfunction (Shah, et al., 2017)

Participants who meet one or more of these criteria will be identified automatically by the Carolina Data Acquisition and Reporting Tool (CDART). Initial eligibility will be reported in both the *Imaging Recruitment Report* and the *Recruitment Snapshot Report*. Site personnel must then verify whether these participants meet any of the following ***exclusion*** criteria that would prohibit them from enrolling in the study.

1. Unable to lie flat for the PYP/HDP scan.
2. Have hypertrophic cardiomyopathy.
3. Have a myocardial infarction in the past 6 months
4. Have dementia or cognitive impairment that precludes them from consenting for the study.

Participant responses to questions that ask about each of these exclusion criteria are documented in the PYP Recruitment and Eligibility (PYRE) form.

If the *Recruitment Snapshot Report* indicates that a participant who is completing an ARIC visit is eligible for the PYP study, then the participant should be given a brochure for the PYP study

and informed they will be contacted by phone in approximately one week (± 5 days). Alternatively, staff may use the visit to discuss the PYP/HDP scan, screen the participant, schedule an appointment, and provide all the necessary documentation including the consent form. If an eligible participant who attends a visit is not given a brochure, then the brochure can be mailed and followed by a phone call that occurs approximately one week later.

## 3.2 INITIAL CONTACT AND SCREENING

When discussing the ARIC-PYP study with a participant for the first time in-person or over the phone, staff should utilize the recruitment script approved by the Institutional Review Board (IRB). The script refers to the PYP Recruitment and Eligibility form (PYRE) form which will need to be updated in CDART after speaking with the participant. This form documents whether a participant who is classified as initially eligible for the study is interested in completing a PYP/HDP scan and whether they meet all the criteria required for enrollment. Additional information about the PYRE form is provided in the Question by Question (QxQ) in CDART.

For the PYP study, participants must be able to consent to the study for themselves. Participants with a low MMSE score or who are known to have dementia will be excluded from the CDART Imaging Recruitment Report, but recruiters are asked to use their judgement in the case that a participant appears to have cognitive impairment or cannot consent themselves for any reason. If the participant is listed as eligible, but appears to have cognitive impairment or cannot consent to the study for themselves for any other reason, mark item 0c as missing in the PYRE, indicate this reason in the notelog, and do not proceed to schedule the participant's PYP appointment.

## 3.3 SCHEDULING APPOINTMENTS

The date and time of each PYP/HDP scan is recorded in the PYRE form. Please note that PYP/HDP scans must be scheduled a minimum of one week from a PET scan for the ARIC Neurocognitive Study (NCS). CDART will provide a warning message if a PYP/HDP scan appointment date is entered that is less than 7 days from a PET scan appointment.

The preferred order is for PET scans to be scheduled before PYP/HDP scans, but this sequence is not required.

## 3.4 REMINDERS

Approximately 5 to 7 days before the scheduled scan, the participant should receive a copy of the consent form. The consent form will be stamped "Do not sign" so the participant will know to review the form but delay signing until the scheduled appointment. The participant should also be sent an appointment reminder letter that includes visiting instructions and a map with directions to the imaging facility.

Approximately 2 days prior to the scheduled scan, staff should call the participant, remind them about their appointment, ask if they reviewed the forms sent by mail, and answer any questions that arise. If necessary, staff can also make special arrangement such as transportation to and from the appointment, assistance in ambulation during the appointment, etc.

In addition, as per the local protocols instituted by health care facilities for COVID-19 screening, participants may need additional screening questionnaires or procedures.

## 3.5 REQUIRED MATERIALS

To complete a PYP/HDP scan, staff will need to bring the following materials.

1. Reimbursement check with signature form for participant and pre-printed social security number when necessary.
2. Written consent form.
3. A printout of the *Recruitment Snapshot Report*.
4. Copy of key forms in case CDART is not accessible. This includes the PYP Clinical Data form (PYCD), Respiratory Questionnaire form (RSX), Physical Exam form (PEX), and PYP Procedure Completion form (PYPC).
5. Copy of this manual.
6. Contact information for Dr. Shah, Dr. Dorbala, and the local Principal Investigator in case there is an unexpected adverse event that requires immediate notification of key personnel on the study.

## 3.6 OBTAINING CONSENT

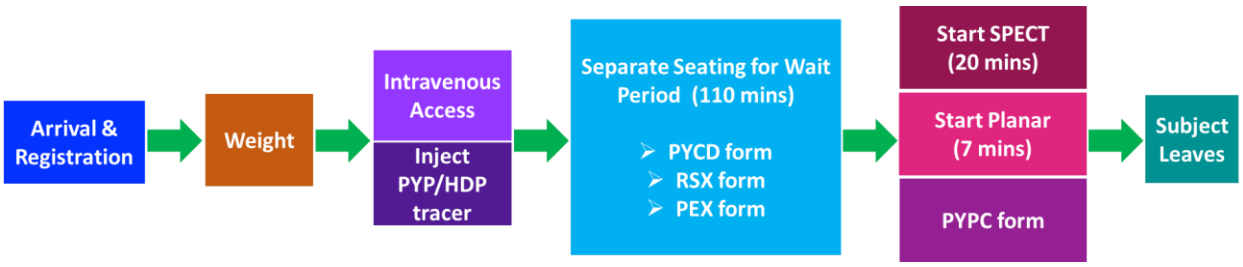
Written consent for the ARIC-PYP study will be obtained at the beginning of the scheduled appointment, following local institutional policies of social distancing and screening procedures for COVID-19. This should be done in a private area with ample time as needed to answer any questions asked by the participant. The content of the consent form complies with guidelines from the National Heart, Lung, and Blood Institute, the ARIC Steering Committee, and the requirements of each field center's IRB. The content is designed to inform the participant of the purpose and procedures of the study and the voluntary nature of their participation. The form makes the participant aware of the right to withdraw from the study, to not participate in a procedure, or to decline to answer any question(s) without penalty.

## 3.7 COMPLETING AN APPOINTMENT

Staff should perform the following steps for the PYP/HDP procedure in the sequence outlined.

1. The participant arrives and completes registration, including written consent, at the front desk following current institutional policies.
2. ARIC staff measures and records the participant's weight.
3. ARIC staff inserts an intravenous access for injection of PYP/HDP.
4. ARIC staff asks the nuclear technologist to inject the radioactive tracer required for the PYP/HDP scan. After the injection, all staff should maintain 6 feet of distance from the participant whenever feasible.
5. The participant is seated in a separate room for the duration of the 110 minute wait-period.
6. During the wait-period, ARIC staff administers the PYCD (PYP Clinical Data), RSX (Respiratory Questionnaire), and PEX (Physical Exam) forms.
7. Walk the participant to the scanner table 10 minutes prior to the scan acquisition time. This can be as early as 2 hrs after injection.
8. The nuclear technologist completes the SPECT PYP/HDP image acquisition which will take approximately 20 minutes.

9. The nuclear technologist completes the Planar PYP/HDP image acquisition which will take approximately 7 minutes.
10. The nuclear technologist fills out PYPC (PYP Procedure Completion) form. ARIC staff enters data from the form into CDART, ensuring that the nuclear technologist's assigned ARIC staff ID number is recorded.
11. ARIC staff addresses any remaining participant questions or concerns before they depart.
12. ARIC staff or nuclear technologist transfers PYP/HDP scan images to the BWH-NRC through the Epernicus software as detailed in Section 7 Data Transfer below.




Detailed instruction for completing the PYCD, RSX, PEX, and PYPC forms are provided in the QxQ. When necessary, the order in which forms are administered may be rearranged. However, the injection of the radioactive tracer should always be performed as soon as possible so that the participant does not have to wait longer than necessary while the injected radiotracer travels through their body. Staff should maintain 6 feet of distance from the participant whenever feasible.

Any errors made on either form should be marked by placing a single line through the error and placing initials next to the correction. CDART can also be updated if paper versions of the forms are not being utilized. To protect participant confidentiality, the participant ID should be used on the forms. The participant ID should also be entered into the scanning machine for the imaging.

### 3.8 RECRUITMENT GOALS

The goal for the study is to complete 225 PYP/HDP scans per site for a total of 900 scans. Recruitment rates will be reviewed monthly and if any modifications are required in the recruitment procedures, these will be considered based on achieved rates.

## 4 PYP/HDP SCAN INFORMATION

The potential risks to subjects from the PYP/HDP scan are minimal. Each participant will be exposed to radiation from $^{99m}$Tc-pyrophosphate/$^{99m}$Tc-Oxidronate 15 mCi (dose range 14 mCi - 18 mCi). The average amount of radiation is estimated to be up to 3.8 milliSieverts (including a CT for attenuation correction when applicable), which is equivalent to what the participant would normally receive in 1.2 years from natural sources.

The average PYP/HDP scan appointment is approximately 3 hours. This includes a 2 hour waiting period after the PYP/HDP radiotracer is injected and 30 minutes of imaging time for the PYP/HDP scan. If scan quality is determined to be unacceptable, the scan must be repeated while the participant is still present. Due to limited budgets, there are no funds for rescanning during a repeat appointment.

If the participant experiences discomfort during the PYP/HDP scan, every effort should be made to make adjustments that will allow scan continuation. If the participant elects not to complete the scan, then the PYP/HDP scan must be abandoned and the local Study Coordinator must be notified.

# 5 PYP SCAN PROCEDURE

$^{99m}$Tc-PYP/$^{99m}$Tc-HDP acquisition and reconstruction will be performed locally at ARIC centers using study-specific protocols. 15 mCi of $^{99m}$Tc-PYP/$^{99m}$Tc-HDP will be injected, followed 120 minutes later by SPECT or SPECT/CT and planar chest imaging (scan time: ~ 20 minute SPECT and ~ 7 min planar). Digital images and SPECT or SPECT/CT data will be electronically transferred to the Nuclear Reading Center at Brigham and Women's Hospital (Boston, MA). The images will be analyzed by visual and detailed semi-quantitative approaches using regions of interest on the myocardium, lungs, and blood pool. Attenuation corrected SPECT images will be used when available.

# 6 QUESTIONNAIRES

During this visit, clinical questionnaires focused on amyloidosis related history will be administered. Dyspnea will be assessed using the modified British Medical Research Council (mMRC) scale, which describes 5 grades of dyspnea (Launois, Barbe et al. 2012) and classified as none (mMRC grade 0), mild (grade 1-2), and moderate-severe (grade 3-4).

# 7 DATA TRANSFER

PYP/HDP scans will be transferred from Field Centers to the BWH-NRC electronically using the Epernicus system.

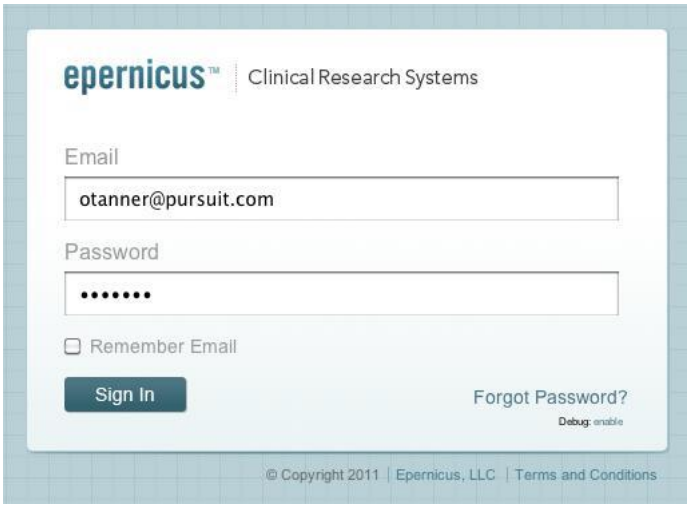
Transfer of completed scans to the Reading Center has the following components:

1. Upon finalizing a PYP/HDP study, the nuclear technologist would save all the necessary scan images to a local temporary PACS or a permanent archive following site specific protocols. We recommend the DICOM images be stored on an institutional archive for at least 8 weeks or until confirmation from the NRC that images are received and interpretable.
2. DICOM images are deidentified using the site initial (M, F, J, W) followed by 6-digit ARIC subject identifier (eg., F123456; M345678; J123456). The DICOM images must include the PYP study image acquisition date. Based on institutional procedures, the deidentified images can be uploaded by the nuclear medicine technologist to the Epernicus system following steps listed below. If that is not feasible, DICOM images can be saved on a CD and the ARIC staff/study research coordinator can upload the images to Epernicus. <u>All participant identifiers except ARIC ID and study date must be removed before sending images via Epernicus.</u>
3. For each PYP/HDP scan performed and transmitted to the BWH-NRC, the nuclear technologist must also separately fill the PYPC datasheet.

4. Field center staff must submit the PYPC datasheet and all other electronic case report forms via CDART and PYP/HDP images from the PACS in a DICOM format via Epernicus to the BWH-NRC as outlined below. Please note that information from the PYPC datasheet will also need to be entered into Epernicus.
5. Due to firewalls at several institutions, it is easiest to transfer image files as one compressed "zipped" file. The easiest way to compress a zip file is to navigate to the files on your computer or disc, highlight them all, Right-click, and under the "Send To" menu select compressed/zipped folder. If your files are on a CD/DVD you will be given a prompt that a zip file cannot be created on the disc and the computer will ask if you would like to send the folder to the desktop. Click 'Yes'. The zipped folder should now appear on your Desktop.
6. Use process for uploading and transferring studies via Epernicus as documented below.

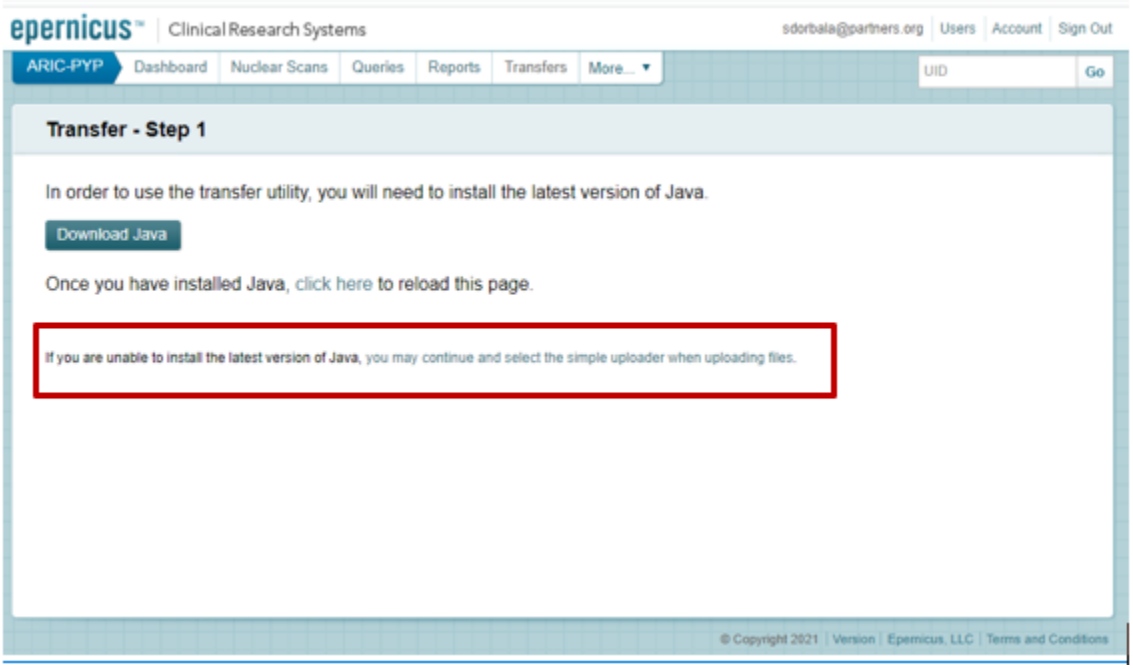
**Instructions for Electronic Transfer of Scans to the BWH-NRC using Epernicus**

1. Sign in: Navigate to https://epernicus.partners.org and sign in with your email address and password (provided to you by the BWH-NRC)

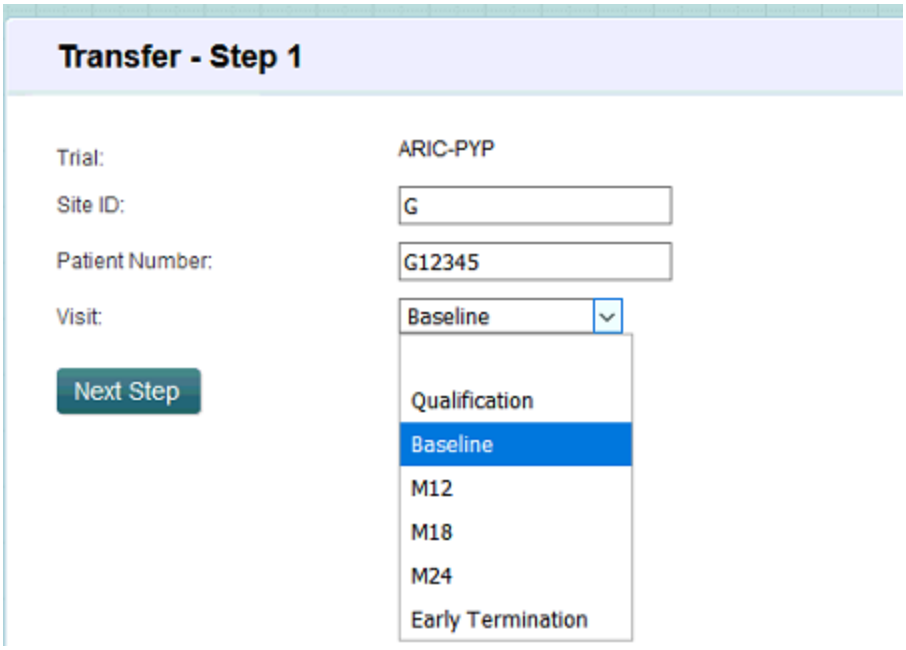


2. Initiate new PYP datasheet: Click on “New Transfer” to begin process

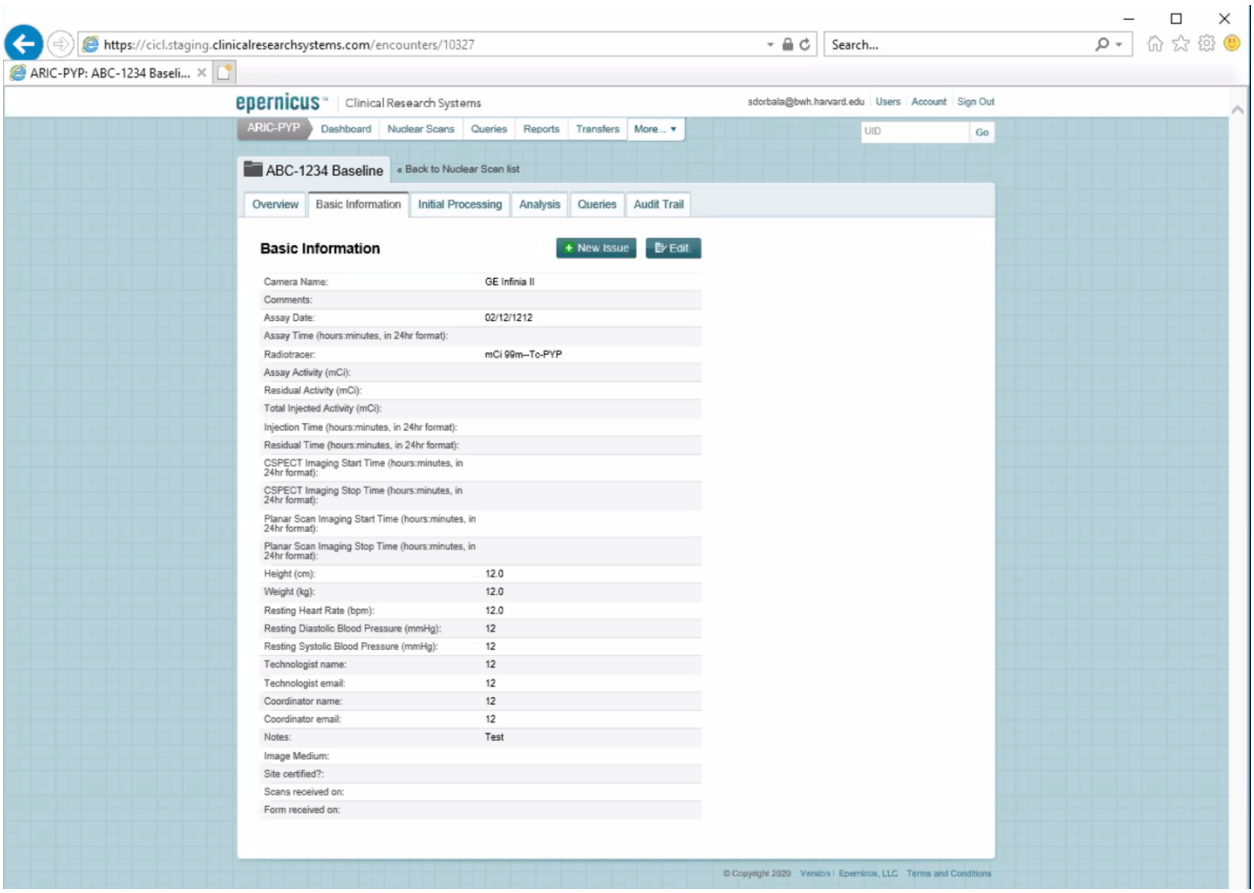

3. On the following screen, you will be prompted to download Java. Many institutional firewalls block Java download. Therefore, do not click on the “Download Java” button. Instead, click on the “you may continue and select the simple uploader when uploading files” text on the last line of the page (indicated by the red box on the image below).



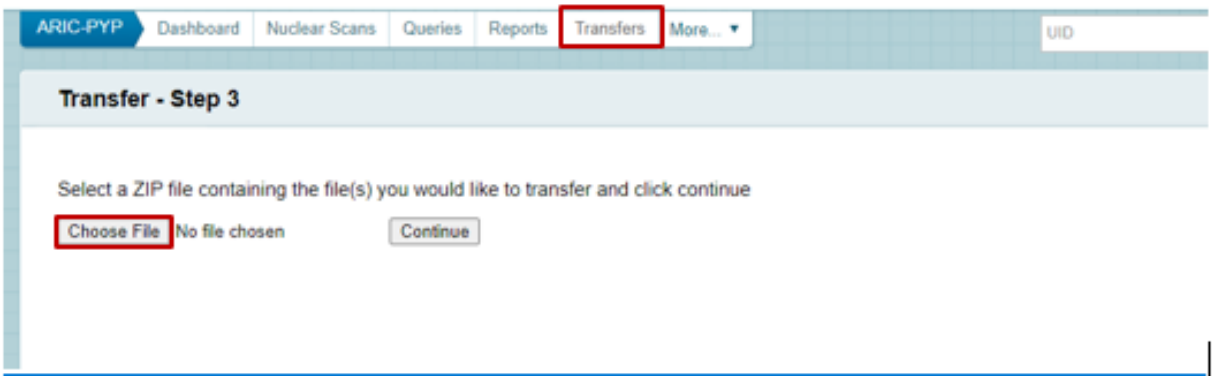
4. Enter participant ARIC ID You will select your site identifier (one of ‘F’, ‘J’, ‘M’ and ‘W’) and enter the 6 digit Subject ID. Select Visit as Baseline from the dropdown menu. Then click “Next Step”.

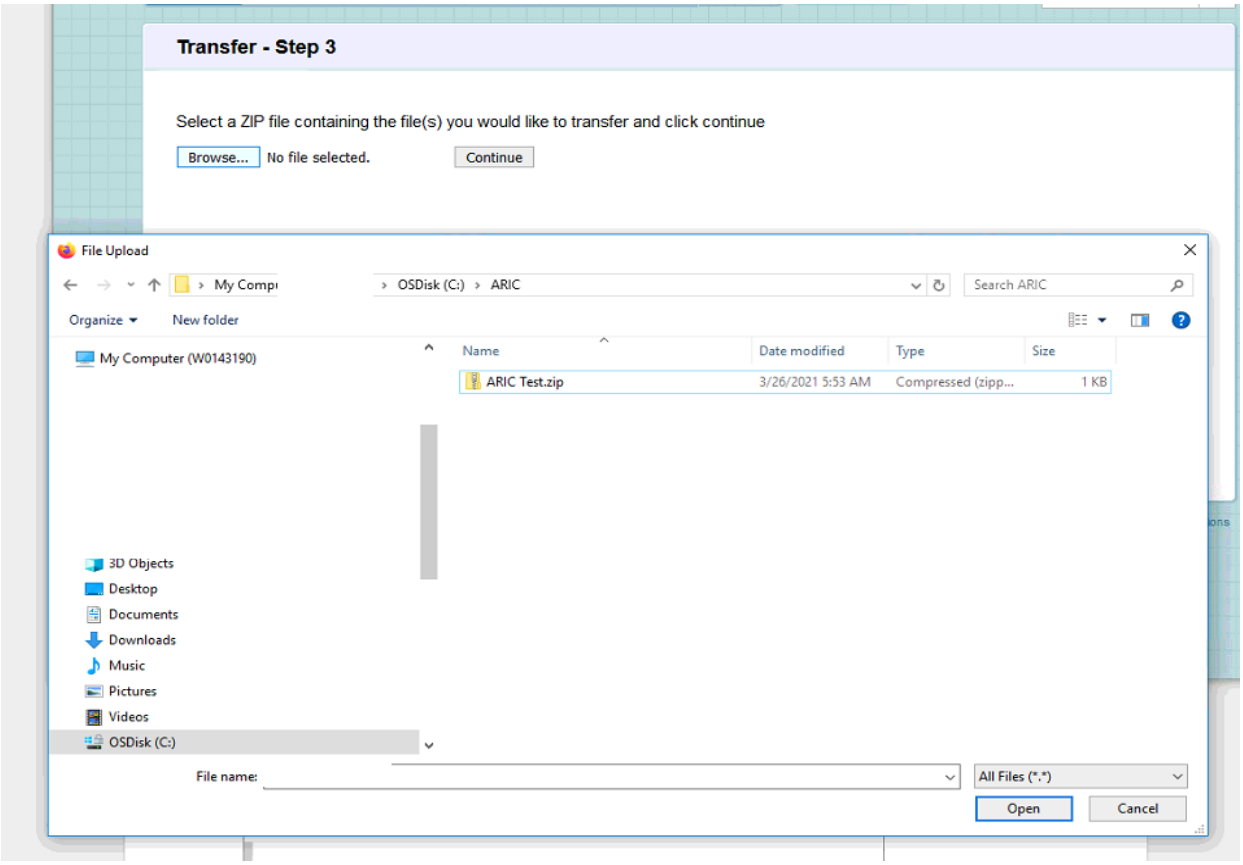


5. You will now be taken to the Basic Information page. Enter required data. All fields are required and are validated according to type. If the data for certain fields are unavailable, you can select ‘N/A’ from the menu to the right side of that field to indicate that it is intentionally left blank (sample screen shown below). (Note: This information will also be entered into CDART.) When done, click “Next Step”.

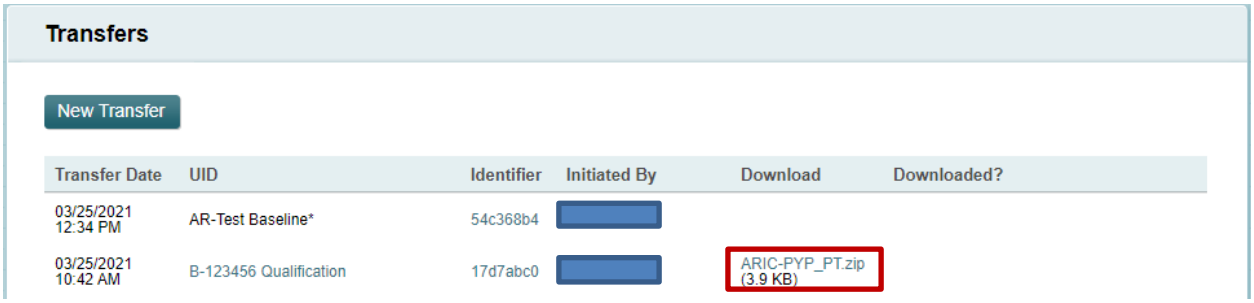


6. On the next page, click on “Choose File” and navigate to the zip file on your Desktop. After uploading the zip file click ‘Continue’ button.

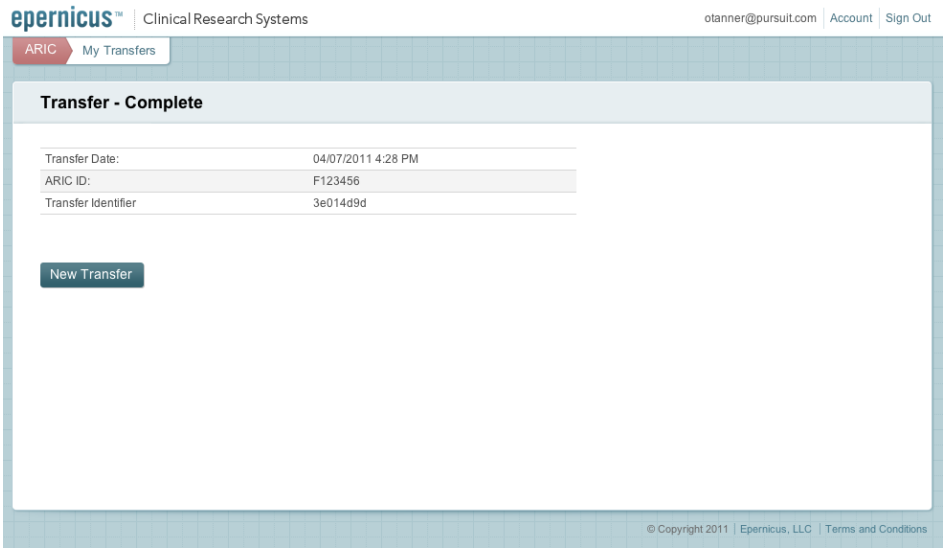


7. To ensure an image was successfully uploaded please check your transfer tab (located on the top of the screen as outlined in red in the image above). The download column on the right hand side (see image below) should show an image file that can be downloaded from Epernicus by the NRC. In the image below, Row 1 has no image file listed in the download column. Row 2 shows an image file listed- this is what you should see if your image file were successfully uploaded.




8. 'Transfer compete' confirmation screen
    - You can initiate another transfer, click on "My Transfers" to view your transfer history




You will also receive an email confirming transfer is complete. For questions regarding either scan performance or submission, the BWH-NRC has an established "hot line" channel of communication, which is listed within the Field Center PYP/HDP Scan Manual of Operations.

# 8 DATA MANAGEMENT

Not applicable

# 9 TRAINING AND CERTIFICATION

### 1. Scanner Qualification

The purpose of scanner qualification is to ensure consistent, high-quality PYP/HDP scans are performed study-wide. Each site must be certified before initiating participant recruitment. Certification is obtained by submitting the scanner qualification form to the BWH-NRC.

Scans will be scrutinized for adherence to protocol, acquisition and processing of all required views, and image quality. Itemized direct written feedback and suggestions will be provided from the BWH-NRC to the chief nuclear technologist for the particular site. This is intended to address any individual equipment or operator dependent problems that may arise.

### 2. Nuclear Technologist Qualification

ARIC PYP/HDP scans will be performed by qualified nuclear medicine technologists who will be specifically trained by BWH-NRC staff and certified on the ARIC PYP imaging protocol.

### 3. ARIC Field Center Staff Training

ARIC field center staff should review the PYP/HDP manual and PYP/HDP data collection forms to familiarize themselves with this protocol. Field Center staff should also review ARIC Manual 2 for general interviewing techniques and complete the listed certification requirements contained therein for the PEX and RSX forms.

# 10 QUALITY CONTROL

The below quality control measures will be evaluated.

1. The dose of Tc-PYP/Tc-HDP is 15 mCi (range 14-18 mCi).

2. Time between PYP/HDP injection and scan is consistent with ARIC-PYP/HDP protocol (120 minutes).

3. Patient motion will be evaluated on the rotating projection images.

4. Image counts on the planar image contains at least 1,000,000 counts.

**BWH-NRC Feedback to Field Centers**

In situations where concerns arise regarding the quality of a scan, the Field Center Coordinator and the nuclear technologist site supervisor will receive BWH-NRC Generated Poor Quality Feedback and Queries via email. The BWH-NRC and the performing nuclear technologist will also receive a copy of this notification. This feedback will include technical instructions for quality improvement. Field Centers should respond to queries as soon as possible but no later than 10 business days. The query will contain easy to follow instructions for how to resolve key issues. Field Centers should contact the BWH-NRC with questions related to queries received.

# 11 REPORTING OF STUDY RESULTS

Key findings of the PYP/HDP scans will be reported to the participants and/or site investigators typically within weeks of scan acquisition and transmittal. We do not anticipate any critical findings on the PYP/HDP or low dose attenuation correction CT scans.

Overreading physicians at BWH-NRC may identify specific non-critical abnormalities that would be important for a participant and physician to be aware of, but that don't necessarily require emergent care. These findings will be incorporated into the routine data transfers from the BWH-NRC directly to the Data Coordinating Center. Such findings include a) ancillary findings on the lung CT scan i.e. lung nodules, pleural effusion, aortic or pulmonary artery dilatation, b) unexpected ancillary findings on PYP/HDP scan.

# 12 REFERENCES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# 13 Appendix

## ARIC-PYP Ancillary Study
## PYP/HDP Scan Protocol Document

**I. Instructions for Conducting Studies**

**II. Guidelines for Image Optimization**

**III. Submission of Studies from the Field Center to the Reading Center**

**IV. Tc-99m-pyrophosphate/Tc-99m-Oxidronate Acquisition and Reconstruction Protocols**

**V. Results Letter Template – ARIC-PYP/HDP Study**

**VI. Technetium-99m-pyrophosphate (99mTc-PYP)/ Technetium-99m-Oxidronate (99m-Tc-HDP) CPT codes**

**VII. Contact Information**

# I. Instructions for Conducting Scans

### A. Qualified Scanners

An acquisition ARIC PYP/HDP default for the ARIC-Amyloidosis Ancillary Study will be programmed in each nuclear scanner incorporating the parameters listed in the Section V.

### B. Participant Identification on Recorded Images

The BWH-NRC should receive no participant identifiers, such as the name, on actual PYP/HDP scan images. Record only the participant's 6 digit ARIC study ID.

### C. Participant Preparation

- Participants do not need to fast for the PYP/HDP scan.
- The participant should be imaged in the supine position with both arms (or at least the left arm) raised above the shoulder.
  - When a dedicated SPECT scanner without CT is used (e.g., Jackson Site), the participants **must** be able to raise both arms (or at least the left arm) above the shoulder.
  - When a SPECT/CT scanner is used (e.g., Forsyth County, Minneapolis, and Washington County), if the participant is unable to raise both arms above the shoulders, they may be imaged with arms by their side.
- Participant's should be instructed to not move during scan acquisition.
- PYP/HDP images should be obtained in a manner that is most consistent with good participant care.
- Participant care issues, including participant comfort, should always supersede research interests. A pillow maybe placed under the head and a wedge under the knees for comfort.
- Participant cooperation and comfort are extraordinarily important in obtaining the highest quality PYP/HDP scan.

# II. Guidelines for Image Optimization

ARIC qualified scanners and ARIC specific PYP/HDP imaging protocols should be used to optimize image quality (Section V).

# III. Submission of Scans from the Field Center to the BWH-NRC

Each site will be responsible for assigning the appropriate ARIC participant ID to each scan. Other identifying information **should not** be transferred to BWH-NRC. Each Field Center will download the PYP/HDP scan images from local PACS and transfer to the BWH-NRC. The images should include raw and reconstructed data for planar and SPECT, and attenuation correction CT images (when applicable).

An example of the image list is shown below for a SPECT-CT scanner:

| Name | File | File Type |
|---|---|---|
| PYP/HDP Chest | Planar static | DICOM |
| PYP/HDP Tomo | Chest SPECT Tomo (160 views) | DICOM |
| PYP/HDP Tomo | Advanced (quantitative file) | DICOM |
| PYP/HDP Tomo | Non-AC Recon | DICOM |
| PYP/HDP Tomo | AC Recon | DICOM |
| PYP/HDP Tomo | Isotope A-Recon-NoAC (primary photopeak energy window for scatter correction for QC) | DICOM |
| Attenuation correction | CT scan B08s | DICOM |
| Attenuation correction mu-map (pixel value is the actual attenuation coefficient) | CT scan 5.0 B08s (slice thickness to match PYP/HDP images) | DICOM |
| Chest CT | CT scan 3.0 B31s | DICOM |
| Dose report | CT DLP | DICOM |
| Topogram | CT scan 1.0 T80s | DICOM |
| Patient protocol | CT and PYP/HDP dose | DICOM |

An example of the image list is shown below for a SPECT scanner:

| Name | File | File Type |
|---|---|---|
| PYP/HDP Chest | Planar static | DICOM |
| PYP/HDP Tomo | Chest SPECT Tomo (160 views) | DICOM |
| PYP/HDP Tomo | Non-AC Recon | DICOM |
| PYP/HDP Tomo | Isotope A-Recon-NoAC (primary photopeak energy window for scatter correction for QC) | DICOM |
| Patient protocol | PYP/HDP dose | DICOM |

For each site, the nuclear technologist and field center staff will be provided with login and password to the Epernicus system. The images should be transmitted electronically from the Field Centers to the BWH-NRC using Epernicus (secure web transfer system) within 2 days. The steps for image transfer are detailed below in Section 7: DATA TRANSFER: Instructions for Electronic Transfer of scans to the BWH-NRC. Field center staff will receive electronic confirmation by email upon successful receipt of each PYP/HDP scan by the BWH-NRC. The nuclear technologist performing the PYP/HDP scan is responsible for completing the PYPC scan datasheet that contains information on participant weight, dose of radiotracer injected, and times of scanning for each PYP/HDP scan (Page 1 of form below). Page 2 of the PYP/HDP datasheet includes the details of the PYP/HDP scan protocol for reference. Each site must submit the information from the PYPC scan datasheet via CDART. At the end of the study, all scans should be transferred to the local picture archiving and communication system (PACS). The DICOM images may be submitted to Epernicus by the nuclear medicine technologist or by the ARIC study research coordinator, based on site specific protocols. The Epernicus web transfer system will also require completion of data captured on the PYPC scan datasheet. PYP/HDP images may be acquired using ARIC participant ID or using full patient identifiers based on site specific protocols. The DICOM images transmitted to the BWH NRC must be fully deidentified using only ARIC participant ID and must include the date of the PYP/HDP Image acquisition.

## $^{99M}$TECHNETIUM-PYROPHOSPHATE (PYP)/OXIDRONATE (HDP)

### IMAGING PROTOCOL: Cardiac Planar and Chest SPECT

**(Please follow below protocol and call (617)732-6647 or (617)732-6290**

**if there is any change)**

$^{99m}$Tc-PYP/HDP dose range: (14 mCi -18 mCi). Print radiotracer sticker and stick below. Start scan 120 minutes after injection of PYP/HDP

**I. Chest SPECT imaging first:**

- Position: Supine
- Both arms raised above shoulders
- 180-deg detector configuration
- 20-minute scan (40 views/detector, 30 sec/view)
- 3 lead ECG gated
- Scatter window

**II. Chest planar imaging next (patient can take a bathroom break after SPECT scan):**

- Position: Supine
- At lease left arm raised above shoulders
- 90-deg (Anterior and Lateral)
- 750,000 counts (~7 minutes)
- Ungated

**III. Reconstruction (specific for the site):**

- Static SPECT images
- Gated SPECT images (8 gates)
- Planar images

# IV. Tc-99m-pyrophosphate/Tc-99m-Oxidronate Acquisition and Reconstruction Protocols.

Below are the generic parameters that will be optimized for each site and scanner specifically.

**Scan Type and Start time:** There will be 2 acquisitions (a planar and a SPECT) after a single radiotracer injection, including:

- Chest SPECT/CT scan: Start 2-hour post injection ± 15 min
- Chest Planar scan: Start 2-hour 15 min post injection ± 15 min

**Radiopharmaceutical:** Technetium-99m-pyrophosphate ($^{99m}$Tc-PYP), preferred/ Technetium-99m-Oxidronate ($^{99m}$Tc-HDP) alternate during PYP shortage

**Dose:** 15 mCi

**Route of administration**: Intravenous

**Patient Preparation**: No specific preparation (Not fast required)

**Camera:** SPECT/CT (preferred) or SPECT (allowed)

**Acquisition and Reconstruction:**

**Gantry set up**: 180-degree collimator configuration
90-degree setup for static image (anterior and left lateral)

**Patient setup**: Supine position, arms above head if able, with entire chest in the field of view

**Planar Acquisition Parameters:**

A. Chest Static 750k counts
B. Simultaneous ANTERIOR and LEFT LATERAL IMAGE
C. Magnification: 1.0

**SPECT Acquisition Parameters:**

A. Matrix: 128 x 128
B. Collimator: low energy high resolution (LEHR)
C. Photopeak: 140 keV with 20% window
D. Scatter window: 80 keV
E. Image zoom: 1.00
F. Camera Preset: SC- TC$^{99m}$-NMG
G. Detectors: Both Detectors 180-degree angle
H. Orientation: Head out
I. Patient Position: Supine
J. Rotation Direction: Clockwise
K. Starting Angle: 0
L. Number of Views: 40

M. Time per View: 30 sec
N. Detector Configuration: 180
O. Orbit: Noncircular
P. Mode: Step and Shoot

**SPECT Reconstruction Parameters:**

A. Iterative Reconstruction
B. Flash 3D (or similar if available)
C. Range: 180
D. Subsets: 6
E. Iterations: 10
F. Attenuation Coefficient: 0.15
G. Automatic Contours
H. Projection Angles: 2
I. Edge Strength: 0.5
J. Background Threshold: 5
K. Kernel: 3x3
L. Gaussian Filter: 8.40
M. Zoom: 1.0

**CTAC:** A CT for attenuation correction is acquired (CTAC) after the SPECT**. **Please shrink CT field of view to only cover the heart****

A. Topogram: (*Cardiac slow Adult)*
B. mA: 20
C. kV: 120
D. Slice: 1.0mm
E. Delay: 3 sec
F. Tube position: Top
G. Scan direction: Craniocaudal
H. API: None
I. Kernel: T20s standard
J. Window: Topogram Body

CTAC Acquisition parameters:

A. Eff. mAs: 44 CARE Dose 4D
B. kV: 110
C. Slice: 5.0 mm Acq. 6 x 2.0 mm
D. Delay: 3 sec
E. Number of Images: 47
F. Pitch: 0.75
G. Scan direction: Craniocaudal

CT Reconstruction parameters:

*A. CT Chest 5.0 B08*
B. Kernel: B08s SPECT AC
C. Window: Mediastinum
D. FoV: 500 mm
E. Image order: Craniocaudal
F. Recon increment: 5.0 mm

G. *CT Chest 5.0 B31s*
H. Kernel: B31s medium smooth
I. Window: Cardiac
J. FoV: 500 mm
K. Image order: Craniocaudal
L. Recon increment: 5.0 mm

Shift images to CT if necessary and save.

**Image Preparation for Transfer**

**Whole Body Scan**:

Anterior-Posterior and Lateral Chest Planar DICOM images should be submitted to the BWH Nuclear Reading Center with no filtering.

**SPECT Scan**:

If you use attenuation correction, please submit both attenuation-corrected and –uncorrected images. For non-attenuation corrected SPECT images, reconstruct images using the parameters given above. For uncorrected images, standard filtered back-projection (FBP) should be used with a Butterworth low-pass pre-filter. The slice thickness should be approximately one pixel. The reconstruction filter parameters listed above may vary with vendor. Do not use ECG gating for the SPECT acquisitions. Send us ungated raw data and reconstructions, both using a 128x128 matrix.

# V. Results Letter Template – ARIC-PYP/HDP Study

Dear [NAME]:

Thank you for taking part in the ARIC-PYP Study. This was the heart scan you had using a radiotracer called <99mTc-PYP, 99mTc-HDP>to detect cardiac amyloidosis, an abnormal protein that can accumulate in the heart muscle.

[If Negative scan based on 'Visual Score' variable] There are several types of cardiac amyloidosis. The heart scan you underwent only tests for one type that is called ATTR amyloidosis, and is the most common type to occur in your age group.

The scan you had performed was for research purposes only. **Your scan fortunately showed no evidence of ATTR cardiac amyloidosis.** The visual grade of radiotracer uptake was [grade 0/1], and indicates no significant ATTR amyloid in the heart.

[If Positive scan based on 'Visual Score' variable] **Your heart scan displayed evidence of ATTR cardiac amyloidosis.** This finding should be discussed with your physician, as follow-up studies and/or treatment may be warranted. The visual grade of radiotracer uptake was [grade 2/3] and is consistent with detectable ATTR deposition in the heart. Given these results, further evaluation with genetic testing and/or blood and urine test for light chain amyloidosis should be considered in discussion with your physician.

[If text present in 'CT Findings' variable]: The following incidental findings were noted on the CT scan imaging performed during your heart scan. Please review these with your physician as follow-up may be necessary: [INSERT 'CT Findings' TEXT HERE]

[If text present in 'Comments' variable]: [INSERT 'Comments' TEXT HERE]

We are grateful for your time and effort as a member of ARIC.

Sincerely,

<signature>

<Name, date>

# VI. Technetium-99m-pyrophosphate ($^{99m}$Tc-PYP)/ Technetium-99m-oxidronate CPT codes

Suggested CPT codes:

Tc-99m PYP SPECT plus planar: 78803

Tc-99m PYP/HDP radiotracer: HCPCS Level II code A9538

# VII. Contact Information

For technical PYP/HDP scan-related questions, please direct all questions and inquiries to the Brigham and Women's Hospital Nuclear Reading Center:

| | |
|---|---|
| Project Coordinator: | Jocelyn Canseco Neri, MS<br>Alexandra Epstein, BS |
| Telephone: | (617)732-6647<br>(617)732-6290 |
| Fax: | (617)582-6056 |
| Email: | jcanseconeri@bwh.harvard.edu<br>Aepstein3@bwh.harvard.edu |
| Address: | ARIC PYP Study (PI: Dr. Sharmila Dorbala)<br>BWH Nuclear Reading Center<br>ASB1-L1, Nuclear Medicine<br>75 Francis Street<br>Boston, MA 02115<br>USA |