Manual 34
MRI and PET Procedures
ARIC-NCS III

Version 0.4 – 03/13/2023

MRI and PET Procedures

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0 REVISIONS

Version Number	Date	Author	Section(s)	Description of Update
0.1	Jan. 5, 2021	Pike	All	Initial MRI and PET Procedures Manual
0.2	Mar. 9, 2022	Nguyen	3.1	Included guidance for identifying participants for MRI in ACHIEVE. Added Appendix 1 for MRI results template letters.
0.3	Dec. 2, 2022	Nguyen	3, 6	Updated Section 3 to identify participants requiring Block A Neurocognitive assessment during the remainder of MRI and PET Imaging. Updated Section 6 to include updated results for neurocognitive testing, template letters are available in Appendix 2.
0.4	Mar. 13, 2023	Nguyen	3, 3.4	Updated Section 3 to clarify the administration of the partial neurocognitive testing during the remainder of MRI and PET Imaging. Removed references to Visit 11 Telephone in Section 3. Updated Section 3.4 to include language about the partial neurocognitive exam in relation to the scheduling of an imaging appointment.

1 LIST OF ABBREVIATIONS

ARIC	Atherosclerosis Risk in Communities
CDART	Carolina Data Acquisition and Reporting Tool
DICOM	Digital Imaging and Communications in Medicine
IRB	Institutional Review Board
IVF	PET Imaging Visit form
MPC	MRI Procedure Completion form
MRI	Magnetic Resonance Imaging
MRE	MRI Recruitment and Eligibility form
NCS	Neurocognitive Study
PET	Positron Emission Tomography
PRE	PET Recruitment and Eligibility form
QxQ	Question by Question

2 OVERVIEW

This manual of operations provides an overview of recruitment and assessment procedures for magnetic resonance imaging (MRI) and positron emission tomography (PET) for the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS). Specific details about these procedures that are pertinent to MRI and PET technologists are described in ARIC Manual 13 (MRI Procedures) and ARIC Manual 31 (PET Procedures).

ARIC participants are eligible for MRI and PET scans regardless of whether they have had prior brain imaging. Recruitment and consent procedures for MRI and PET scans are combined since participants must complete both scans.

MRI and PET procedures are conducted utilizing standardized protocols. These protocols will be identical across participants. The same MRI sequence and the same version of the PET scan will be completed for each participant. All personnel must be fully familiar with this manual of procedures, be trained and certified in the appropriate protocols, and remain standardized 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.

3 RECRUITMENT AND ASSESSMENT SEQUENCE

Most ARIC participants who enroll in the ARIC-NCS Brain Imaging Study will have 8 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. If the participant agrees to take part in the study, appointments for an MRI scan and a PET scan will be scheduled.
3. Participant receives an appointment reminder letter, appointment location map, local MRI screening form, and a copy of the consent form approximately 5 to 7 days before the scheduled MRI scan.
4. Participant receives a reminder call approximately 2 days before the MRI scan.

5. Participant signs the consent form and completes the MRI scan.
6. Participant receives an appointment reminder and appointment location map approximately 5 to 7 days before the scheduled PET scan.
7. Participant receives a reminder call approximately 2 days before the PET scan.
8. Participant completes the PET scan.

The steps involved with each of these interactions are described in Section 3. Please note that the order of scans can be swapped, with the PET scan occurring before the MRI scan. In that situation, the consent form must be signed at the appointment for the PET scan.

Neurocognitive Testing during MRI and PET Imaging Data Collection

Participants eligible for and interested in MRI *or* PET during the Visit 10 period of data collection and have not completed neurocognitive testing in the past year will receive the partial neurocognitive battery and CDP. Staff may refer to the *V10 Snapshot Report* to determine who should receive the assessment.

The options for completing the partial neurocognitive assessment may occur on the same day as the imaging exam or as part of the clinic Visit 10. Recruiters for MRI or PET imaging should inform psychometrists about the required testing.

3.1 IDENTIFICATION OF POTENTIAL PARTICIPANTS

CDART Imaging Recruitment Report

Participants who are initially eligible for an MRI and/or PET Scan can be identified by using the *Imaging Recruitment Report* in the Carolina Data Acquisition and Reporting Tool (CDART). A participant is classified as initially eligible if they do not have a known contraindication, such as implanted metal. Review the Imaging Recruitment Report Guide in CDART as needed.

The information generated by the *Imaging Recruitment Report* is also provided in the *Recruitment Snapshot Report*. If the *Recruitment Snapshot Report* indicates that a participant attending a visit is initially eligible for an MRI and/or PET scan, then the participant should be given a brochure for the ARIC-NCS Brain Imaging Study and informed they will be contacted by phone in approximately one week (+/- 5 days). Alternatively, staff may use the visit to discuss the MRI and PET scans, screen participants, schedule appointments, and provide all the necessary documentation including the consent form, local MRI screening form, etc. 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.

ACHIEVE MRI

The Imaging Recruitment Report includes ACHIEVE MRI eligibility, which includes different eligibility criteria from ARIC-NCS Brain Imaging Study. Participants eligible for ACHIEVE MRI will be recruited for an MRI scan by ACHIEVE recruiters, per the ACHIEVE protocol.

3.2 INITIAL CONTACT AND SCREENING

When discussing the MRI and PET scans 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 MRI Recruitment and Eligibility (MRE) form and the PET Recruitment and Eligibility (PRE) form which will need to be updated in CDART after speaking with the participant. These forms document whether a participant who is classified as initially

eligible for the study is interested in completing an MRI and PET scan and whether they meet all the criteria required for enrollment. Additional information about these forms are provided in the Question by Questions (QxQs) in CDART.

Unlike prior imaging studies, participants with dementia will not be automatically excluded. As a result, recruitment may occur by speaking with individuals who serve as proxies for the participant. For additional information about recruitment via proxy, please refer to Manual 2 (Home and Field Center Procedures).

3.3 ADDITIONAL SCREENING

In addition to the MRE and PRE forms, staff may need to complete a local MRI screening form specific to their MRI imaging facility. Local screening forms will not be available in CDART. However, they should be completed in advance of a scheduled appointment to decrease the likelihood that an unexpected exclusion is identified shortly before a scan. If the eligibility of the participant is unclear after completing the MRE, PRE, and local screening form, explain to the participant that you need to verify if they are eligible and will contact them again soon. In some cases, staff may be required to send a completed version of the local form labeled with the participant ID to the imaging facility prior to the scheduled appointment.

Note: At the Washington County field center, if there are any positive responses to the "welding" MRE question or if there are any questions about responses (particularly for aneurysm, stent, and heart valve questions), please contact staff at Diagnostic Imaging Services (DIS) (Washington County site) to confirm eligibility for the MRI scan. They have proposed that they will fund and arrange for same-day orbital x-rays if needed for welders.

3.4 SCHEDULING APPOINTMENTS

The dates and times of scheduled MRI and PET scans are recorded in the MRE and PRE forms. In most cases, MRI and PET scans will be scheduled on different days. However, MRI and PET scans may be scheduled on the same day if that is preferred by the participant and logistically feasible given the locations and timing of available spots of the MRI and PET imaging facilities.

The preferred order is for MRI scans to be scheduled before PET scans, but this sequence is not required. Regardless of the order, MRI and PET scans should be scheduled within 3 months of each other if possible.

During Visit 8 and Visit 9, MRI and PET scans should be scheduled within 6 months of an in-person or phone-based neurocognitive assessment. During the remainder of the MRI and PET data collection period that takes place during Visit 10, participants will receive the partial neurocognitive battery and CDP if the participant is eligible and expresses interest in an MRI or PET scan and has not received a neurocognitive test in the last year.

When scheduling an appointment with the local imaging facility, the participant ID should be utilized. The name of the participant should *not* be entered.

Most imaging facilities allow studies to reserve regular scanning slots. To achieve the recruitment goals for this study, it is recommended that each site reserve at least 2 slots in a row for MRI scans 2 to 3 days a week. A similar schedule will be required for PET scans. It is especially important that 2 to 4 PET scans to be scheduled in a row as this is more cost efficient for transporting the PET isotope. A potential timetable for completing back-to-back PET scans with two participants is provided below.

Table 1. Potential Timetable for PET Scans with Two Participants

Procedure	Time	
	Participant #1	Participant #2
Written consent (if applicable)*	1:00	1:45
Weigh participant*	1:20	2:05
IV insertion, injection, then remove IV lines**	1:30	2:15
Participant goes to restroom	2:10	2:55
Position participant supine on PET scanner table**	2:15	3:00
Scan Acquisition** (50 minutes after injection)	2:20	3:05
Scan Transition** (70 minutes after injection)	2:40	3:25
Participant goes from PET scanner table to prep room.**	2:45	3:30
Discharge participant	2:50	3:35

*Completed by ARIC field center staff
**Completed by PET technologist

Please note that most imaging facilities have a cancellation policy in which notification is required one day to one week in advance. Cancellations will also require notification by the close of business the night prior to the PET scan as well as notification of PETNET, the company that makes and transports the PET isotope. Either field staff or PET technologists will need to contact PETNET to order a dose of the PET isotope in advance of each PET scan. Ideally, this will occur at least 5 days before the PET scan. Consequently, it is critical for field staff and PET technologist to accurately gauge and monitor the number of doses needed from week to week. The process for coordinating these orders will vary from site to site and should follow similar procedures and timing to those used in the ARIC-PET study.

3.5 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. If applicable, the participant can also be provided with the local screening form required by the imaging facility and asked to complete the form in advance of their appointment.

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.

3.6 REQUIRED MATERIALS

To complete an MRI 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. Local MRI exclusion form.
4. Copy of the MRI Procedure Completion (MPC) form in case CDART is not accessible.
5. Copy of this manual.
6. Contact information for Dr. Gottesman and the local Principal Investigator.

To complete a PET scan, staff will need to bring the following materials.

1. A scale to measure the weight of the participant on the day of the PET scan. Please note that this is not necessary if a scale is available at the imaging facility.
2. Reimbursement check with signature form for participant and pre-printed social security number when necessary.
3. Written consent form.
4. Copy of the PET Imaging Visit (IVF) form in case CDART is not accessible.
5. Copy of this manual.
6. Contact information for Dr. Gottesman and the local Principal Investigator.

3.7 OBTAINING CONSENT

Written consent for both the MRI and PET scan will be obtained at the beginning of whichever scan is initially completed by the participant. This should be done in a private area with ample time to answer any questions asked by the participant. Please note that since the consent form describes both the MRI and PET scan it only needs to be signed during the first appointment. Nonetheless, staff should always have a copy of the consent form available in case a participant who previously signed the form has additional questions at their second appointment.

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.

All participants will be presented with the same consent form. If a participant agrees to only one type of scan, then they should only complete the corresponding section of the consent form. When necessary, consent can be obtained by proxy. For additional information about consent via proxy, please refer to Manual 2 (Home and Field Center Procedures).

3.8 COMPLETING AN APPOINTMENT

During an appointment for an MRI scan, staff will complete the MPC form. For information about completing this form see the MPC QxQ. For additional details about the MRI procedure see ARIC Manual 13 (MRI Procedures).

During an appointment for a PET scan, staff will complete sections of the IVF form. For information about completing this form see the IVF QxQ. For additional details about the PET procedure see ARIC Manual 31 (PET Procedures).

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 a paper version of the MPC or IVF form is not being utilized.

To protect participant confidentiality, the participant ID should be used on the MPC form and IVF form. The participant ID should also be entered into the PET machine and MRI machine.

3.9 FOLLOW-UP PHONE CALLS

Participants who fail to arrive for a scheduled appointment or who cancel their appointments are contacted by phone to reschedule. At that time, staff should attempt to address any concerns the participant may have as well as resolve barriers to participation. A common barrier is fear of radiation from the isotope injected before the PET scan and from the images themselves. If this

is a concern expressed by the participant, it may help to mention that the total amount of radiation is equivalent to the amount received from a Chest CT scan, which is a common medical procedure. Another way to describe the amount of radiation is to say that it is equivalent to 2.5 years of exposure to natural background radiation from such sources as the sun.

Although there is no required routine phone call after imaging procedures, any expected or unexpected adverse events from the PET scan should be recorded in the IVF form in CDART. If the participant reports a serious adverse event, notify the Principal Investigator. For additional information about adverse event protocols, addressing unanticipated problems, and handling medical emergencies please refer to Manual 2 (Home and Field Center Procedures).

If any adverse event occurs during the PET scan, staff may choose to conduct a follow-up phone call with the participant approximately 2 days later. The need for this follow-up call will be at the staff member's discretion. In most cases, it will not be necessary but if the participant seems especially concerned or had any new symptoms post-PET scan, a call should be considered. The outcome of this call should be recorded in the PET Imaging Visit (IVF) form.

3.10 RECRUITMENT GOALS

The goal for the study is to complete 1000 MRI and PET scans across sites. Recruitment rates will be reviewed monthly and if any modifications are required in the recruitment procedures, these will be considered based on achieved rates.

3.11 TRAINING AND CERTIFICATION

Staff are certified centrally by way of a webinar describing the procedures outlined in this manual. Supplemental training will be provided through the Brain Imaging Recruitment Subcommittee. Training for MRI and PET technologists are described in ARIC Manual 13 (MRI Procedures) and ARIC Manual 31 (PET Procedures). For new staff hired after the study initiation, experienced staff will perform an on-site training. Two recruitment calls will need to be performed under the supervision of a previously certified staff member before that new staff member is considered certified.

Recruitment rates will be reviewed at all sites on a monthly basis. Additional training may be scheduled as necessary if recruitment rates are especially low for specific staff members.

4 MAGNETIC RESONANCE IMAGING (MRI) INFORMATION

The average MRI scan is approximately 30 minutes. 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 in the MRI, every effort should be made to adjust the table, head coil, etc. to allow scan continuation. If the participant elects not to complete the scan, then the MRI scan must be abandoned and the local Study Coordinator must be notified.

Each site will be responsible for anonymizing participant information according to local laws and regulations. Once this is done, data can be transferred to the reading center.

For additional details about MRI procedures, please refer to ARIC Manual 13 (MRI Procedures).

5 POSITRON EMISSION TOMOGRAPHY (PET) INFORMATION

During a scheduled appointment, the weight of the participant must be measured and entered into the IVF form in *pounds*. This should be done approximately 30 minutes prior to the planned

Amyvid (florbetapir, AV-45) injection, so should be done at the PET center. Weight can be measured utilizing a scale at the imaging facility or a scale brought by staff. For situations where there is a problem or excessive delay with delivery of the Amyvid tracer, and the scan has to be rescheduled, the weight should be repeated on the day that the PET scan takes place.

An intravenous (IV) injection is performed by a PET technologist utilizing a standard sterile protocol. After the IV is placed and the Amyvid (AV45/florbetapir) is injected, staff should relocate to the waiting room or imaging room. To avoid exposure to recurrent radiation, staff should *not* remain in the same room as the participant.

The imaging facility may provide radiation monitoring tags that must be worn by staff. These tags will be periodically monitored, as per routine for PET centers, to assure safe levels of exposure to radiation. The radiation monitoring tags should be kept at the PET facilities. The amount of anticipated radiation exposure is quite low.

Scans will be obtained after a 50-minute uptake period. The actual PET scanning time is 20 minutes. Once the scan is completed, staff will ask if the participant noticed any adverse effects. Responses will be recorded on the IVF form. The site or overall Principal Investigator should be notified about any serious adverse effects, with the site PI notified about other adverse events.

Each site will be responsible for anonymizing participant information according to local laws and regulations. Once this is done, data can be transferred to the reading center by the PET technologist. For additional details about PET procedures, please refer to ARIC Manual 31 (PET Procedures).

6 REPORT OF STUDY RESULTS, MEDICAL REFERRALS, AND NOTIFICATIONS

To better serve participants, MRI results that have established value for medical diagnosis or treatment are summarized and provided to the participant and his/her physician when permission is granted (see Appendix 1). PET results will not be provided as these results do not have specific clinical meaning and are not informative for diagnosis or treatment.

Participants who receive the partial neurocognitive battery during the MRI and PET Imaging data collection at Visit 10 will receive testing results. The results are summarized and provided to the participant and his/her physician when permission is granted (see Appendix 2).

The MRI results and neurocognitive testing results are provided in the CDART *MRI Summary of Results Report*. Any available MRI results or neurocognitive testing results are displayed in the report, regardless of the presence of another test during the report run date.