Standard Operating Procedures for General MRI Acquisition

Accelerating Medicines Partnership® SCHIZOPHRENIA

An observational study examining clinical trajectories and predictors of outcomes in the clinical high risk population.

Version 1.2, 21 SEP 2024

Procedure	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visit 15	Visit 16	Conversion
Month	-3 to -1	0	1	2	3	4	5	6	7	8	9	10	11	12	18	24	-
Consent Form	✓																
Interview/ Questionnaire	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Cognitive Tasks		✓		✓				✓						✓		✓	✓
MRI*		✓		✓													
EEG*		✓		✓													
Blood and Saliva Samples*		✓		✓													
Actigraphy (daily)		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Digital Data (daily passive sensing, EMA, audio diary)		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
Free Speech Sampling (audio and facial recording)		✓		✓													
PSYCHS (audio recording)		✓	✓	✓	✓			✓						✓	✓	✓	✓

** In-person visit*

AMP SCZ MRI Acquisition – General

Standard Operating Procedure (SOP)

Version 1.2; Effective Date 2024-09-21

I. Scope

This document is a general overview of MRI Acquisition for AMP SCZ that applies to all 3 scanner vendors — Siemens, General Electric, and Philips. The sessions for each participant will consist of structural T1- and T2-weighted scans, three dMRI scans, four resting state functional scans (rfMRI), and scans for field (distortion) mapping. The output of an imaging session will be the scan data and the completion of an online "MRI Run Sheet" (with annotations on the imaging session) in the appropriate network (PRESCIENT or ProNET) database.

II. Responsibilities

AMP SCZ Imaging Core

The AMP SCZ imaging core is composed of imaging experts from PRESCIENT, ProNET and DPACC and will be responsible for:

- Training the site staff at the start of every study. Detailed training procedures/requirements are elaborated below.
- Reviewing all test data generated during the site qualification, including data upload procedures to the DPACC.
- Ensuring each site is qualified with an operating imaging protocol and data upload procedures before any participants are scanned.
- Monitoring the quality and accuracy of the data obtained.
- Provide ongoing technical support to help sites resolve technical issues that may occur along the study, including requalification in cases of major software/hardware upgrades.

Site Personnel

The site personnel at each site will have responsibilities related to MRI scanning of participants. These responsibilities include:

- Designate primary contacts at the MR imaging center (typically the lead MR technologist) and clinical/research site (typically the study coordinator).
- Recruiting individuals according to the study protocol.
- Ensure that all participants have signed the appropriate ethics committee approved informed consent form before they are scanned.
- Scheduling the MRI scans in compliance with the study protocol.
- Ensure that all participants pass MRI screening and preparation according to the local site requirements.
- Explain the protocol and procedures to participants prior to scanning.
- Acquire the MRI images according to the imaging protocol.

- **Actively review the images during the scan session** in order to ensure the data is of sufficient quality. If there is an issue, please perform a rescan immediately, in order to avoid missing data, or the need to schedule an additional scan date for acquiring replacement scans.
- Complete the online "MRI Run Sheet" with appropriately *specific and detailed* notes regarding any deviations, issues, or problems for the session in either REDCap (ProNET) or RPMS (PRESCIENT).
- Upload the MRI data to the appropriate network database and **confirm** successful upload.

It is the responsibility of the primary contact to ensure the site staff is aware of their role and responsibilities in the study. Also, the primary contact should inform the Imaging Core of any changes in:

- Personnel
- Scanner hardware/software
- Other changes that affect the procedures described in this guide

Communications

The main method for communicating with your site on MRI related matters will be via e-mail to the contact at the MR imaging center and the study coordinator. For matters regarding eligibility and safety, this will be the study coordinator. In some cases, if it is a more urgent manner or a more convenient method for you, we will contact you by phone. During site qualification, the level of interaction will be more regular, as we will be providing instructions about how to perform the study and request some test data from your site.

III. Site Qualification

Prior to any participants being scanned, each site must successfully complete all steps of site qualification. The main purpose of the site qualification process is to ensure that:

- The scanner is capable of acquiring high quality data according to the protocol, and that the site is able to correctly upload the data.
- Each member of the site team understands their role and responsibilities in the study and all the procedures and expectations of the study.

This will ensure that the site is capable of acquiring imaging data that is appropriately high quality. A diagram of the site qualification process is shown below in Figure 1.

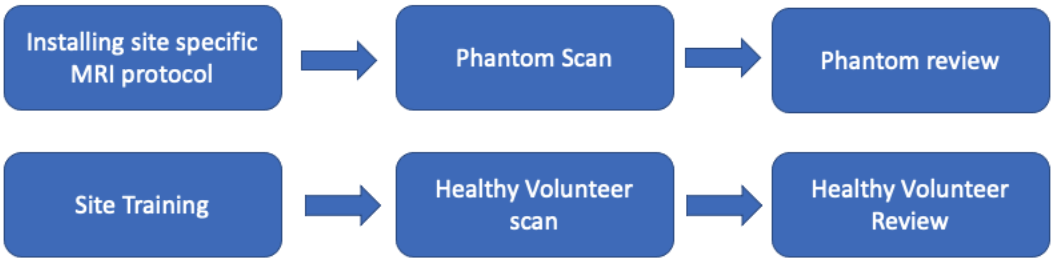


Figure 1. Steps required for site qualification.

The first row in figure 1 defines the steps required to assure that the protocol has been correctly installed on the scanner. The second row assures that the site personnel is thoroughly acquainted with the protocol and trained appropriately to be able complete a scan that fulfills the imaging requirements.

ALL MRI scans conducted on participants must be done on scanners qualified for this study. Except for exceptional circumstances, we will qualify only one scanner per site. ALL participant scans must be performed on this scanner. Any intent to deviate from this must be discussed first with the DPACC and will be handled on a case-by-case basis.

The steps in Figure 1 are detailed further below:

Installing site specific MRI protocols: The Imaging Core will provide the image acquisition protocol specifically for the scanner at your site. The protocol will be provided in an electronic portable format that can be *directly imported/installed* on your scanner. This action should be performed by a trained MRI user (e.g., an MR technician). As part of this process, document any error messages or changes reported by the system, and report those messages back to the Imaging Core. The protocol is NOT to be instantiated via manual set-up from a printout (PDF) of the protocol. If you cannot load the protocol, communicate this to the Imaging Core.

Phantom session and review: Once the imaging protocol has been successfully imported into your MR scanner, collect a test session using this protocol on a phantom and send the data to the Imaging Core. We will review to ensure the protocol has been imported correctly. As part of this phantom session, document any error messages or other unusual scanner behavior and report to the Imaging Core. As a result of the review process, the Imaging Core may identify the

need for alterations in the imaging protocol, which will require repeating the phantom session and review process.

Site Training: A representative from the Imaging Core will arrange a video conference to train the site personnel before the start of the study, and review the information provided in this SOP and any other training material. Note that site training can be scheduled either before or after the phantom scan, depending on site qualification timelines.

Healthy volunteer session and review: The last stage of site qualification is to scan a healthy volunteer. This allows for review of many aspects of imaging quality that can only be assessed by reviewing human scan data. This healthy volunteer would preferably be someone who is readily accessible and willing to be scanned again in the future at your site should there be changes in the software or hardware, where rescanning would be needed to investigate the impact of such changes. The Imaging Core will review the scans from the healthy volunteer session and will qualify your site if the following criteria are met:

- The parameters used for scanning the healthy volunteer must be identical to those that were approved when used in the phantom.
- The images must be of suitable quality for analysis.

If the appropriate Review Board approval is in place for your site to perform this scan on a healthy volunteer, then please perform this scan as soon as possible.

The MRI should be performed using a 3T scanner. The same MR scanner must be used throughout the study for all participants. The scanner used must be the same scanner that was used in the qualification process.

In the occasion of a software upgrade or a major hardware replacement (e.g., head coil, electronics, gradient coil) notify the Imaging Core, ideally *prior* to the upgrade/replacement. Depending on the type of change the Imaging Core may require additional steps, which may include phantom and/or healthy volunteer scanning. Upon a software/hardware change the site will be temporarily paused from scanning until cleared by the Imaging Core.

Participants will be scanned using a standard head coil. The same coil must be used for all scans on all participants at your site to ensure reproducibility of the images acquired.

IV. Staff Training

Before independently performing a AMP SCZ scanning session, staff members will be trained as follows:

1. Read this SOP and any other associated imaging SOPs.
2. Participate in a training session organized by the Imaging Core (at study initiation), or watch the video of the previously recorded training session (new staff following study initiation).
3. Observe a scan session and associated procedures, as performed by trained study staff or an AMP SCZ investigator, *at least once*.
4. Implement/run a scan session and associated procedures under the direct supervision and training of experienced study staff or an AMP SCZ investigator *at least twice*.
5. Be approved for scanning by an Imaging Core representative or by trained site personnel that was designated by the Imaging Core to perform training to new staff.

A representative from the Imaging Core will arrange a video conference to train the site personnel before the start of the study, and review the information provided in this SOP and any other training material. This training session/video will last approximately 2 hours, and will include:

- Overview of the study goals and organization.
- Overview of the imaging goals of the study.
- Review of the imaging SOPs.
- A step-by-step demonstration of a participant scan and a phantom scan.
- Highlights of potential pitfalls and case scenarios.
- A step-by-step demonstration of upload procedures.
- Q&A

The training is required for any site personnel that will be operating the scanner, or assisting in the operation of the scanner, including MRI technologists, postdoctoral fellows, graduate students or research assistants. In the event that multiple MRI technologists at a site will function as scan 'Operators', it is sufficient for the "lead" technologist assigned to the study to complete the training and then take responsibility that the other technologists are appropriately trained locally.

At the beginning of the study it is expected that the initial staff will participate in the training session conducted by the Imaging Core. For the ongoing phase of the study, sites may need to train new staff members due to staff turnover. New staff are required to also complete items (1)-(5) above. Once they have completed those items, the site PI needs to email the Imaging Core regarding the new team member and to certify that all training as listed above was completed.

V. Before the scan session (Setup & Preparation)

1. Metal and health screening

Follow your imaging facility standards for patient screening and preparation (e.g., metal check, MRI screening forms, dress code).

a. MRI safety and clearance for scanning is to be determined per the local requirements, regulations and practices of each site.

b. Even if sites allow scanning a person with **dental appliances**, we suggest the following guidelines, based on the ABCD Study:

   i. Do not scan (due to very likely significant distortions and low quality):

      1. Any stainless-steel braces or palatal expander (regardless of their location in the mouth)

   ii. Ok to scan:

      1. Braces or palatal expanders that are not stainless-steel (e.g., titanium, silver, ceramic and porcelain)
      2. Cap/s
      3. Crown/s
      4. Fillings

   iii. Ok to scan, but may cause artifacts. Scan quality should be checked carefully during scanning. If poor quality, consult with DPACC regarding next time point:

      1. Permanent retainer (lower retainer may be ok; upper retainer more likely to cause severe distortion)
      2. Spacers

   iv. Removable retainers should be removed prior to scanning.

   v. Document any dental appliances in the general Session Comments box in the online “MRI Run Sheet”.

2. Scanner room preparation

a. Prepare scanner bed, sheets, blankets, foot rest, squeeze ball, etc per the customary procedures of the local site.

b. Confirm that video projection and display equipment is operational (for display of fixation crosshair during rfMRI scans). Display the crosshair for initial positioning purposes.

c. Select appropriate head coil and mirror attachment for your site.

   i. **For sites with the 32 ch head coil, use that coil.**

   ii. Otherwise, use the 64 ch head/neck coil (Siemens sites).

   iii. Coils less than 32 channels are **NOT** allowed (e.g., the Siemens 20 ch head/neck coil is not allowed).

d. Ensure that the scanner host computer is operational.

3. Participant preparation

a. Provide an overview of the protocol and the "flow" of the MR session.

b. If your site has a "mock scanner" available, you are encouraged to use it to help acclimate the participant to the scanning experience.

c. Suggest that the participant go to the bathroom prior to the beginning of scanning.

d. Explain to participants that movement badly damages the quality of MR images. Explain that it is important not to move while the scanner is making sounds, and that this includes not only the head, but that the entire body, including torso/legs/feet, should remain still as well. Explain that participants will be most comfortable, and thus best able to remain still, if they maintain a relaxed muscle tone in their face, shoulders, torso and legs (i.e., don't "tense up").

   If the participant appears restless/fidgety, placing a rolled up towel/blanket over the ankles (with support under knees) can be helpful to reduce leg motion.

e. Explain how consistent breathing with a regular steady rhythm is best. And conversely how deep breathing and 'sighing' should be avoided, as this tends to result in movement of the head, and also leads to artifacts in some of the scans due to inconsistent breathing.

f. Explain how participants will be able to communicate with you.

g. Explain how you will communicate to the participants, and how you will "check in" between scans. Let participants know that you will tell them about how long each scan will last prior to starting it.

h. Explain to participants that communication should be done vocally, and not by head nodding.

4. Participant positioning

a. Provide earplugs/headphones to the participant, per your local site's guidelines for hearing protection.

b. Position the participants so their head and neck are relaxed, but without rotation in either plane.

c. Provide a squeeze ball, and explain its functionality.

d. Please use as much head coil padding as possible to create a "snug, but comfortable fit" within the head coil, to help minimize head motion.

e. Offer support under the back and/or legs to decrease strain on the knees and back.

f. **IMPORTANT:** Make sure the coil is shown as fully connected on the display at the magnet. **Do NOT** load the protocol back on the host computer before the coil is fully connected, and the participant is at Isocenter in the bore.

g. Align the positioning laser on the participant's nasion (bridge of the nose, between the eyes) for every scanning session.

h. Advance the participant to Isocenter.
(Siemens: Confirm that when the table stops, the display shows the position as "0 mm")

i. Confirm that the participant can see the fixation crosshair, and that it is centered vertically and horizontally within their view. Also confirm that the remainder of their view is (predominantly) a black background (i.e., no extraneous, distracting stimuli around the periphery of their view).

5. Music and Video

Playing music or video clips is allowed during all scans, *except for during the resting state fMRI scans*, for which the fixation crosshair needs to be projected.

VI. Participant Registration

The precise details of participant registration will vary between platforms and vendors. Here, we specify the basics that should apply for all vendors:

1. Complete appropriate field for AMP SCZ **Participant** ID (e.g., `WU00007`)
    a. Siemens and GE: "Last Name" field
    b. Philips: "Patient name" field
2. Complete appropriate field for AMP SCZ **Session** ID
    a. Siemens and GE: "Patient ID" field
    b. Philips: "Registration ID" field
    c. Session ID is:
    `<Participant ID> + "_MR" + "_YYYY_MM_DD" + <_#>`, where `YYYY` is the 4 digit year, `MM` is the 2 digit month, and `DD` is the 2 digit day for the date of the scan session, with underscores ('_') separating them, and `<_#>` represents the data collection event for the MR modality on that particular day, counting from 1; e.g.,
    `WU00007_MR_2021_11_05_1`
        i. Note that the order and format for the date portion is `YYYY_MM_DD`. Other variants/formats are NOT acceptable; e.g., YYYYMMDD (no underscores), YYYY-MM-DD (dashes instead of underscores), MM_DD_YYYY (incorrect order) are all not acceptable.
        ii. If the participant needs a short break, continue scanning under the same registration if possible (i.e., under same "Session ID"), so that the scans collected after the break remain part of the same session and are numbered consecutively.
        iii. If it is necessary to complete scanning under a different registration on the same day (e.g., scanner crash that requires re-registration, or completing the imaging later on the same day after an intervening session on a different individual), then increment the `<_#>` portion of the session ID by 1; e.g., `WU00007_MR_2021_11_05_2`
        iv. If it is necessary to complete scanning or re-collect the entire session **on a different day** (e.g., due to participant fatigue, incorrect coil or protocol usage, time constraints, etc.) change the date portion of the Session ID accordingly to accurately reflect the current date. e.g.,
        `WU00007_MR_2021_11_05_1` – session ID for first day
        `WU00007_MR_2021_11_06_1` – session ID for following day

3. Other fields:
    a. “Date of birth”:
    Enter the actual year and month of birth, but set the day of the month to 15.
        i. *This way the participant’s exact date of birth will not be contained as “identifying information” in the DICOMs.*
    b. “Sex”, “Height”, and “Weight”:
    Enter appropriate values.
        i. Safety warning: These fields are utilized for power deposition (SAR – specific absorption rate) estimates – therefore, use actual height and weight.
        Do not use “Other” for Sex.
    c. “Patient position” (or similar) field:
    Select “Head first – Supine” from the pull down menu.
    d. “Operator” (or similar) field:
    Enter the initials of technicians / assistants involved in collecting data for this session. Enter technician (or scanner operator) first and assistant overseeing documentation and quality control second (e.g, “MPH/OSP”)

VII. Imaging Protocol

This section provides an overview of the imaging protocol that is appropriate for all 3 vendors.

For further details specific to running the protocol on each platform, see the platform-specific SOP.

Note that the imaging protocol is highly fine-tuned.
Do NOT make any changes to the protocol without first consulting the Imaging Core.

At all times, two site personnel are required to be present in the scanning room.

If possible, the Imaging Core recommends that the scanner itself be operated by a trained MRI technologist. The second individual will be responsible for Quality Control and documenting events in the online "MRI Run Sheet" in REDCap/RPMS.

The imaging protocol is conceptually organized into different blocks:

1. "Location" block – music/video ok
    a. Siemens: `Localizer, AAHScout, Localizer_aligned`
    b. GE: `3Plane_Loc_SSFSE`
    c. Philips: `SmartBrain`
2. "Structural" block – music/video ok
    a. `DistortionMap_AP`
    b. `DistortionMap_PA`
    c. `T1w_MPR`
    d. `T2w_SPC` (Siemens) or `T2w_CUBE` (GE) or `T2w_VIEW` (Philips)
3. "First rfMRI" block – show fixation cross. (Don't forget!)
    a. `DistortionMap_AP`
    b. `DistortionMap_PA`
    c. `rfMRI_REST_AP`
    d. `rfMRI_REST_PA`
4. "dMRI" block – music/video ok
    a. `dMRI_b0_AP`
    b. `dMRI_dir176_PA`
    c. `dMRI_b0_AP`
5. "Second rfMRI" block – show fixation cross. (Don't forget!)
    a. Same set of scans as First rfMRI block

Note: On the GE platform, the Structural and rfMRI blocks are additionally preceded by a `Calibration` scan.

rfMRI scan details:

Make sure music/video is turned off and fixation crosshair is projected and approximately centered in participant's view, with the remainder of the visual field being a (predominantly) black background**.**
PowerPoint (PPTX) and PNG versions of the fixation crosshair to use for AMP SCZ are available as part of the imaging protocol files.

Instruct participant:

a. "Keep your eyes open, and comfortably keep your visual focus on the center of the cross. You can blink normally. Relax your mind, and maintain steady, consistent breathing. And remember to stay still."
b. "This scan will be about 5 minutes, and I'll check in with you once it is completed".

After each rfMRI scan, ask the participant to assess their alertness/compliance on the following scale (which will be entered into the online "MRI Run Sheet" in REDCap/RPMS for the session):

1 = fully awake and alert
2 = mildly tired, but maintained eyes open throughout run
3 = drowsy; eyes closed occasionally for brief intervals
4 = fell asleep during run

If they indicate their alertness as level 3 or 4, gently remind the participant that the goal is relaxed, eyes open fixation on cross throughout the entire scan.

As a related aside, if the participant happens to fall asleep during the T1w, T2w or dMRI scans, that's fine. But don't explicitly offer or endorse that as an option for participants during those particular scans, since once participants start sleeping during scans, it can be difficult to stay awake during the rfMRI scans.

dMRI scan details:

Music/video can be turned back on if the participant wants.

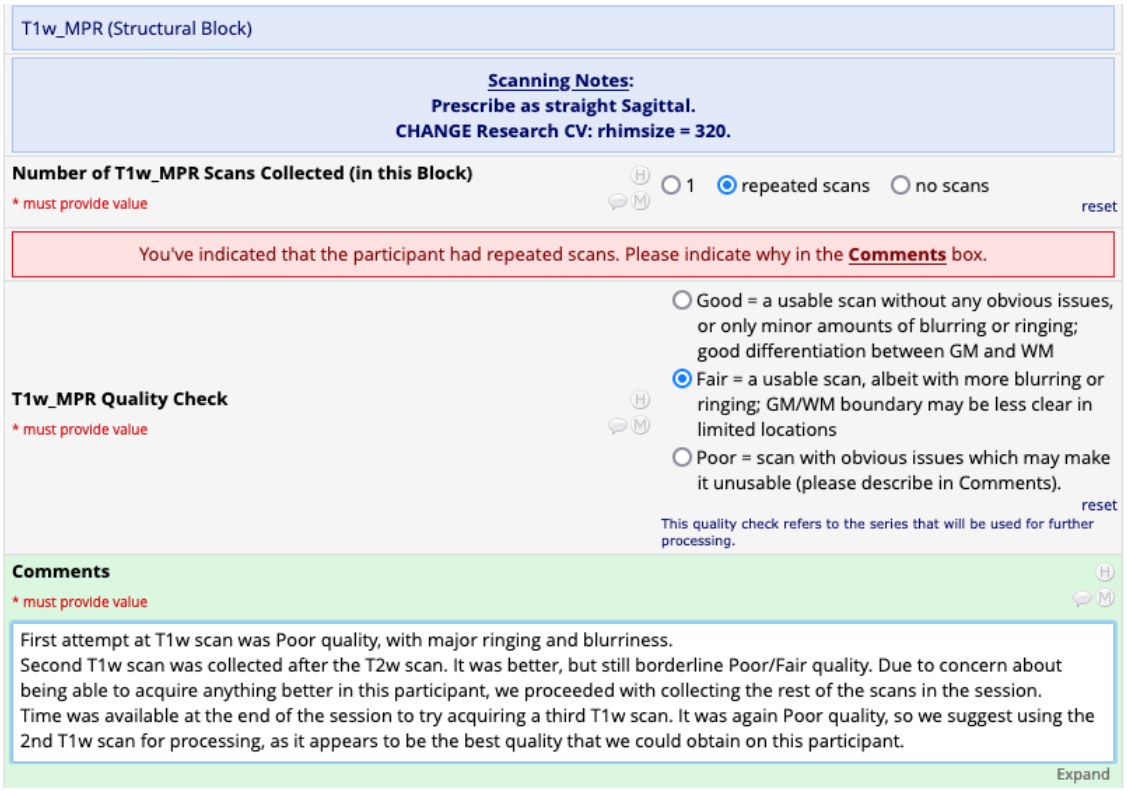
The 3 scans in the dMRI block can (should) be run back-to-back as a consecutive block of 11-12 minutes from the perspective of the participant.

VIII. Documentation

MRI Run Sheet

The online "MRI Run Sheet" in REDCap/RPMS is the official, archival source for documenting and annotating the MR session. If at all possible, the assistant should have the Run Sheet open during the session.

1. This allows real-time entry of detailed, accurate notes *while the session is occurring*, which is the preferred mode for completing the MRI Run Sheet. If this is not possible, sites need to develop a local procedure for ensuring that information and details are not lost between the completion of the session and the filling out of the form.
2. The MRI Run Sheet itself includes helpful built-in reminders for running the session, such as the instructions for the rfMRI scans, and other vendor-customized guidance related to the specific vendor/platform in use for the session.



Example of the MRI Run Sheet for the T1w_MPR scan, with built-in notes customized for the "MR750 (GE)" scanner

3. In the situation of “repeated scans” or “no scans” for a given expected scan in the protocol, a “Comments” box will open, and an explanation must be provided to explain the situation for that particular scan.
    a. Note that in the “repeated scans” condition, the assigned “Quality” value refers to the series/scan that seems best to use for that scan for processing/analysis. This may not necessarily be the last instance of that particular scan, if an earlier acquired scan is deemed to be of better quality. In any “repeated scans” situation, the added Comments need to make clear what occurred and which of the repeated scans is considered to have the best quality.
    b. Please provide detailed and precise notes when prompted with a “Comments” box regarding any scan-level issues or deviations. When in doubt, more text is better.
    c. The above example demonstrates an appropriately clear annotation in a complicated situation in which 3 T1w scans were collected, in which the 2nd of the 3 was deemed to be the best quality (marked as ‘Fair’ quality in this example).
4. The end of the MRI Run Sheet has an “Additional Scan Session Comments” field which is always available, and not linked to any particular scan type, for annotation of any issues related to the overall session, or which simply don’t fit well with a specific scan.
5. **If there is a severe problem/issue in a given session, implying a hardware or software issue of some sort that could re-occur in the next session, *please email the Imaging Core directly*** (in addition to annotating in the Run Sheet appropriately). This is because comments entered into the Run Sheet may not be seen immediately, depending on the bandwidth of the DPACC for reviewing the incoming sessions.

IX. Quality Control (QC)

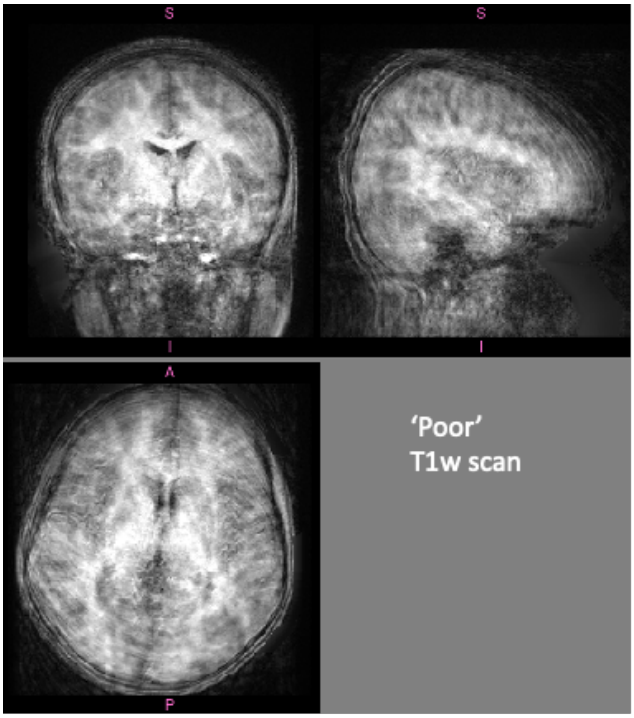
Image quality should be assessed for each series either in real-time (if possible) or shortly thereafter (i.e., as soon as possible during the acquisition of a subsequent scan).

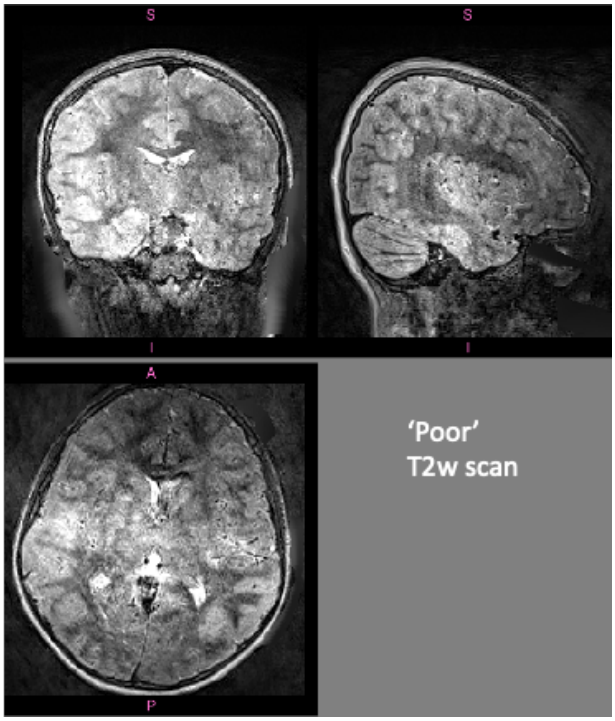
While data quality will be reviewed eventually by the DPACC, real-time QC at the scanner is a very important component to acquiring good quality MR data since:

1. Instructions can be provided to the participant to improve the data quality of the rest of the scans in the session.
2. Poor quality scans can often be reacquired within the same imaging session (time-permitting and participant willing).
3. Possible hardware and/or software issues can be identified promptly, and then investigated and corrected prior to any further imaging sessions.

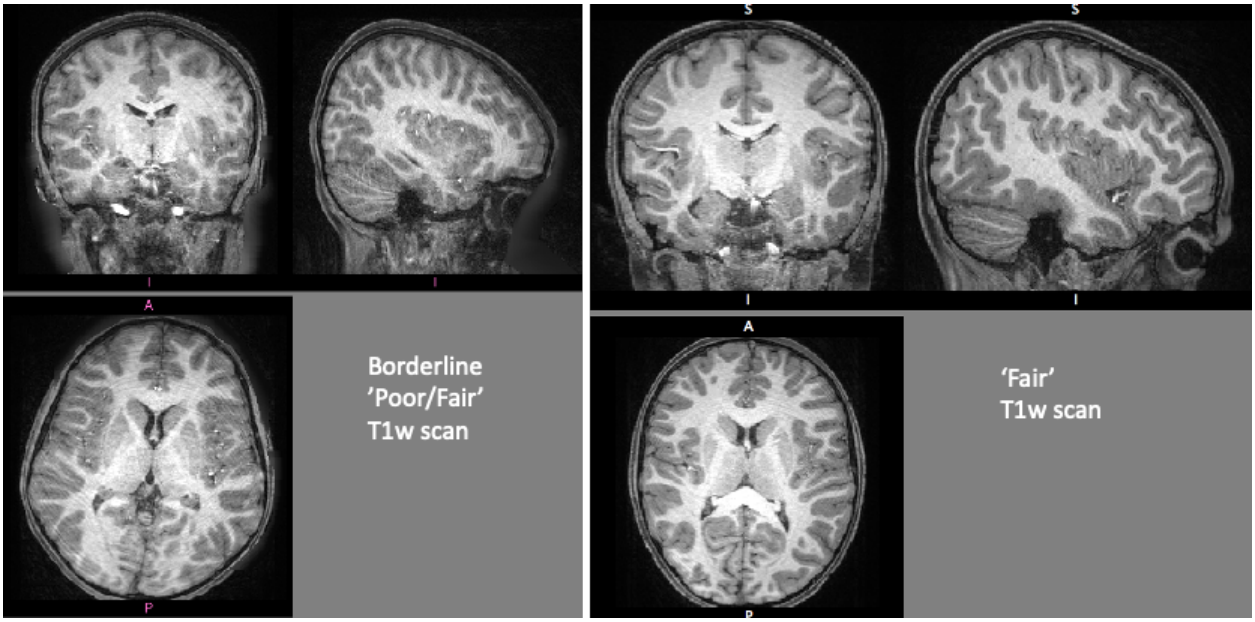
Things to look for as part of the QC within the session include the following:

1. Motion induced artifacts or problems
    a. **When excessive motion is identified, communicate with the subject, remind them of the importance of staying still during scanning (with their whole body, not just the head). Check if the participant is comfortable. Consider if anything else can be done to try to reduce motion** (e.g., adding extra padding; or listening to music or watching a video, if not an rfMRI scan).
2. "Usable" quality T1w and T2w structural scans
    a. All data processing requires a usable T1w scan, and some types of processing require a usable T2w scan. So if the quality of either structural is 'Poor', re-collect that scan immediately. See MRI Run Sheet snapshot above for brief descriptions of 'Poor', 'Fair' and 'Good' quality.
    b. Examples of 'Poor' T1w and T2w scans, which should be reacquired immediately, reminding the participant beforehand of the importance of staying still:

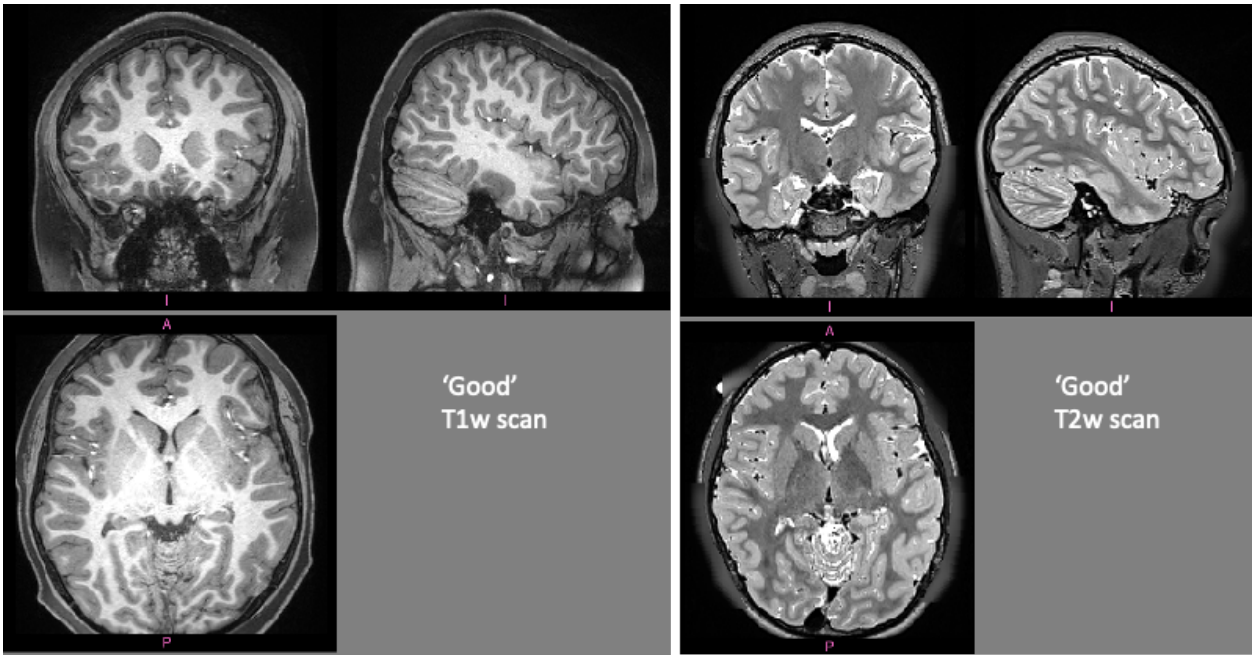




c. Examples of a borderline ‘Poor/Fair’ T1w scan (left) and a ‘Fair’ T1w scan (right). Note the blurriness and lack of a sharp gray/white matter boundary in the borderline scan. such a scan might suffice, if necessary, but this would be a good scan to reacquire, to try to get something better. In contrast, the ‘Fair’ T1w scan on the right has some ringing, but good overall SNR, a crisp appearance, and a clear gray/white matter boundary.



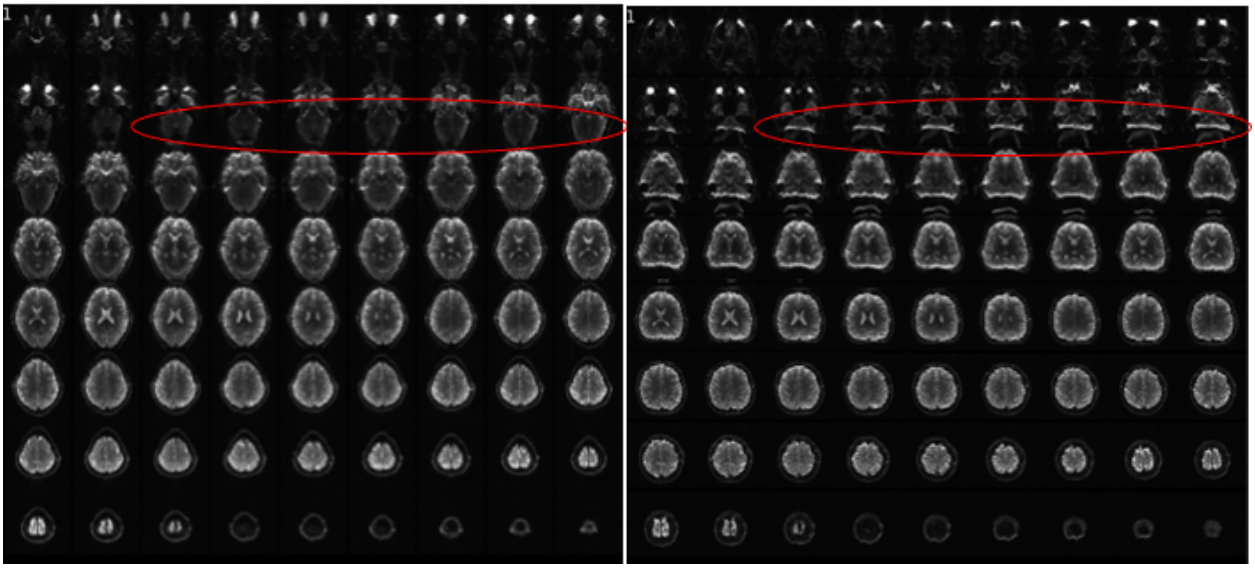
d. Examples of ‘Good’ T1w and T2w scans. There is minimal (or no) ringing, good SNR, and a crisp appearance throughout.



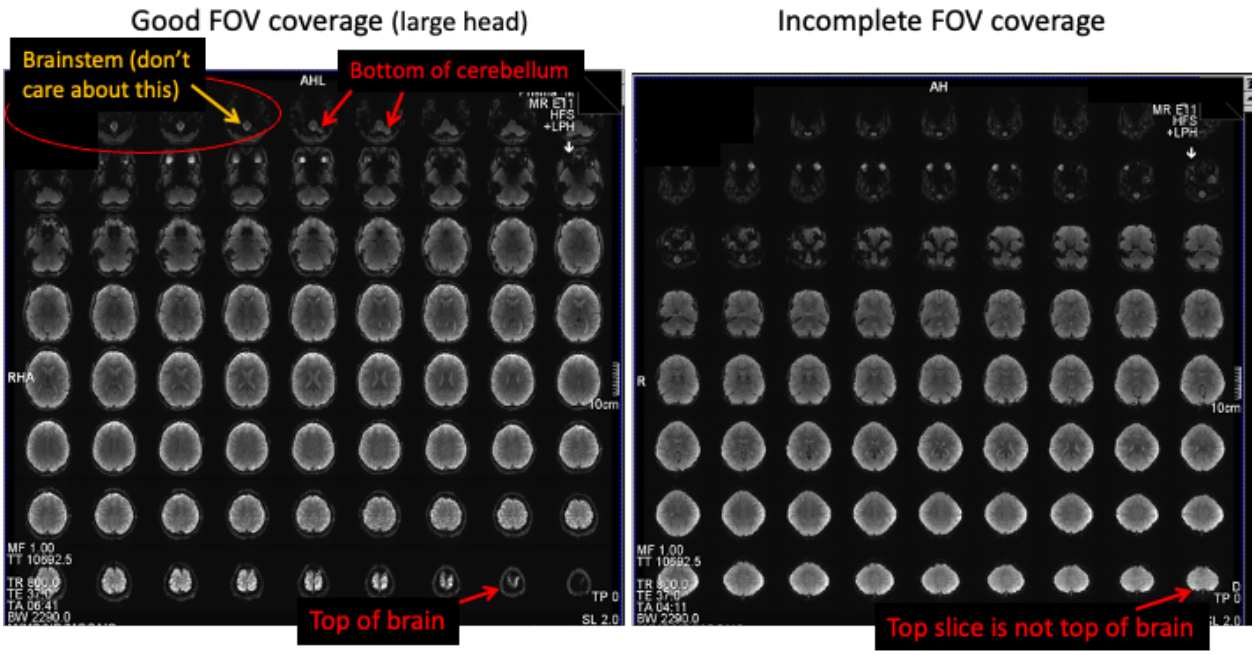
3. Severe (beyond typical) image distortion or signal dropout, especially in the EPI scans (DistortionMap, rfMRI, and dMRI) that are particularly sensitive to susceptibility-induced local magnetic field perturbations.
    a. When observed, remove participant from scanner, and try to identify the source of the distortion (e.g., metal strap on bra, if bra was not removed; hair extensions, pins, beads, dyes, or products; paperclip or other metallic object that found its way into the magnet or coil). Remove/correct the cause of the distortion, if possible, and proceed according to local requirements and practices. If the cause of the distortion is identified and scanning continues, the severely distorted scans need to be reacquired.
    b. "Mosaic"-style views of the EPI data are the best way to conveniently review for distortion (if available), as they show all slices simultaneously.
        i. Example of DistortionMap scans showing severe distortion posteriorly, likely due to a metal bra hook at the back of the neck:

DistortionMap_AP
(excessive expansion posteriorly near cerebellum)

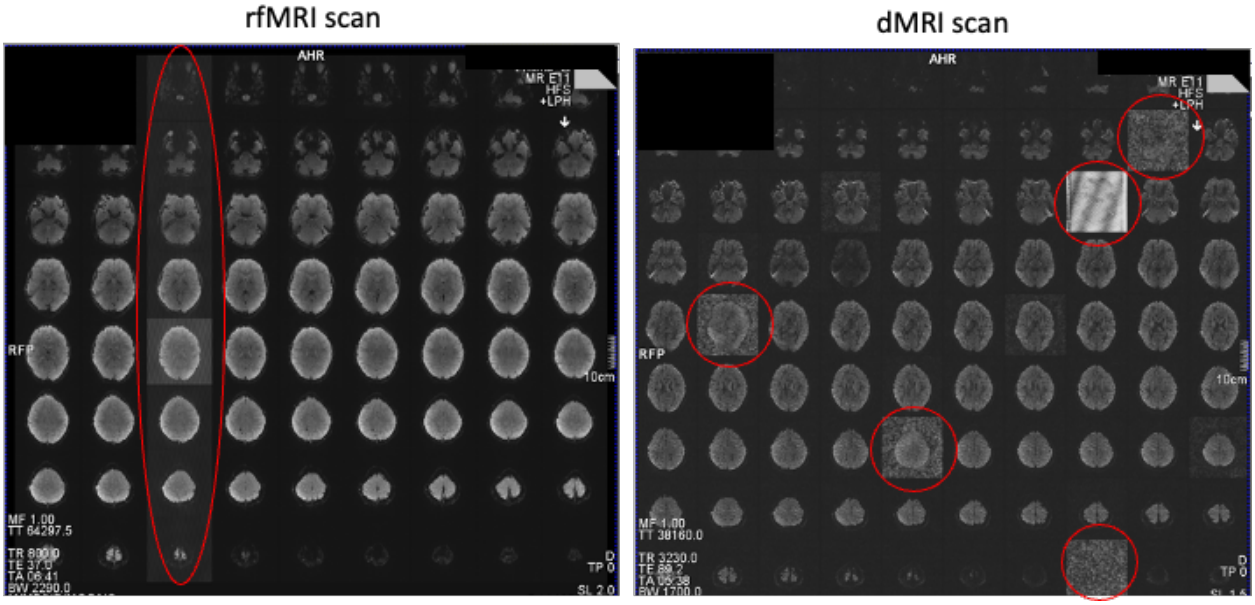
DistortionMap_AP
(excessive compression posteriorly near cerebellum)



4. Is the entire brain (including cerebellum) within the imaging field-of-view (FOV)? Did the participant move out of the FOV over the course of a rfMRI or dMRI acquisition?
    a. If provided by the vendor, use its "inline" or real-time viewing functionality to keep an eye on the quality of the rfMRI and dMRI data as it is reconstructed, both as way to qualitatively assess the amount of participant motion in real-time, as well as to keep an eye on whether the imaging FOV is maintaining coverage of the whole brain.
    b. If the participant moves out of the FOV (which typically would occur by them "sliding out" of the coil), this should be corrected.
        i. It may be sufficient to just instruct the participant to "scootch up back into the coil". See the **Rescan procedures and unscheduled breaks** section below for further details.
        ii. Example of good (left) and incomplete (right) FOV coverage, assessed using mosaic-style view:



5. Spiking or other likely hardware-related issues



6. Ghosting artifact
    a. In each session, adjust the brightness/contrast in at least one rfMRI scan and the main dMRI scan to review the level of background ghosting.
    b. If any structure from the background ghosting starts becoming evident/visible within the brain, that should be annotated within the MRI Run Sheet. If the ghosting seems likely to be due to hardware issues (rather than participant motion), that should be reported to the site's lead MR technician or physicist for further investigation.
7. Fold-over/Wrap-around
    a. Unlikely to be an issue for AMP SCZ, given the size of the FOV, if the FOV is properly positioned. So, if observed, check whether the participant has moved.
8. Reminder: Any relevant QC-related observations should be annotated in the MRI Run Sheet (see **Documentation** section above).
    a. As noted in the **Documentation** section, **if there is any severe problem/issue in a given session, or a question about data quality for which you would like rapid feedback, *please email the Imaging Core directly,*** because comments entered into the Run Sheet may not be seen immediately.

X. Rescan procedures and unscheduled breaks

1. General guidelines

a. Please attempt to collect each scan in the order it is listed in the protocol queue.

b. Please attempt to complete each "block" (structural, rfMRI block 1, diffusion, rfMRI block 2) before taking unscheduled breaks. If the participant requests a break between scans that are members of a "block" (see above), see if it would be possible to finish that block before the break.

c. Continue scanning as time permits.

d. If you must complete or re-collect a session on a different date (e.g., due to participant fatigue, incorrect coil or protocol usage, time constraints, etc.), both the original (if any scans were collected) and rescheduled scanning sessions need to be uploaded to the appropriate ProNET/PRESCIENT imaging database and properly documented in REDCap/RPMS. See data entry instructions for appropriate network (PRESCIENT or ProNET) for how to handle and document this situation of repeated scanning sessions within either the "Baseline" or "Month 2" assessment.

2. "Location" block

a. A participant "Location" is the period of time when the participant is at Isocenter with the brain located within a specific field-of-view (position and angulation) relative to the head coil.

b. **Re-run the "Location" block (defined above for each vendor) in the following situations**:

   i. If the participant's brain (including cerebellum) leaves the field-of-view (FOV), and either (1) it isn't possible to easily restore full brain coverage by a simple verbal instruction (e.g., "please scootch up into the coil"), or (2) even after getting the participant's brain back into the imaging FOV (restoring full brain coverage), it is nonetheless clear that the position/location of the brain is appreciably different from where it was at the start of the session.

      You should be monitoring for this situation by reviewing real-time reconstructions using the vendor's 'inline' viewing option, if available.

   ii. If the participant leaves the scanner (e.g., bathroom break), or you pull the scanner bed from Isocenter to talk to the participant or reposition them.

   iii. If the scanner is rebooted or crashes.

   iv. Note that any time the Location block is repeated, a fresh DistortionMap pair should be acquired as well so that the local magnetic field can be estimated accurately for the new Location.

3. Structural block

a. Preprocessing of ALL scan types requires a structural scan set (pair of T1 and T2 scans) to be usable. If either structural scan is missing or poor quality, *ALL IMAGING DATA WILL BE UNUSABLE*.
   i. Thus, *if the quality of either structural scan is poor, recollect that scan immediately*.

b. An aborted structural scan is worthless, and must be reacquired.

4. First and second rfMRI blocks

a. Within each rfMRI block, it is ideal to collect the two rfMRI scans (with opposing phase encode directions) in the same "Location", if possible.

b. Collecting **complete** scans in **both** polarities yields better overall data:
   i. Opposing phase encoding directions (AP and PA) allows some signal to be recovered in dropout / susceptibility regions
   ii. Resting state connectivity estimates will be less robust with less data (i.e., fewer time points).

c. Aborted rfMRI scans (i.e., scan is discontinued for any reason):
   i. If less than half (50%) of the run is acquired, reacquire immediately.
   ii. If more than three-fourths (75%) of an rfMRI scan is acquired, it is probably best to move-on to acquiring the next scan, and circle back to reacquiring the aborted scan at the end of the session, if time permits.
   iii. If 50-75% of an rfMRI scan is acquired, use your best judgment on how to proceed – if you think there will be time available to reacquire, go ahead and reacquire right away. If uncertain if extra time will be available, proceed to acquiring the rest of the protocol and circle back to reacquiring the aborted scan at the end of the session, if time permits.

d. Preprocessing of an rfMRI scan requires the availability of a DistortionMap pair collected in the same "Location".
   i. Example: Participant needs a bathroom break after the first rfMRI scan in a pair, and *can't wait* until after the completion of the second in the pair. In this case, after the bathroom break you would (1) reacquire the "Location" block, (2) reacquire a DistortionMap pair, (3) acquire the second rfMRI scan in the pair (i.e., REST_PA). This way you have a DistortionMap pair appropriate for each rfMRI scan location.

5. dMRI block

a. All three scans in this block must be collected in the same "Location", and consecutively. Since the `dMRI_b0_AP` scans are relatively short, this should not be a problem. (From the perspective of the participant, it is fine to simply run all 3 dMRI scans in a consecutive fashion, without any pauses in-between.)

b. Aborted dMRI block: Follow same guidance as provided above for the rfMRI blocks (i.e., < 50%: reacquire immediately; > 75%: reacquire at end of session, time permitting; 50-75%: use your best judgment based on how the session is proceeding).

XI. MRI Incidental Findings

Any time the scanning operator or assistant identifies a potential incidental finding (i.e., possible anomaly or concern based on their non-clinical experience) as part of the typical review/QC of the images at the scanner, they should trigger their own institutional procedure for incidental findings in an MR scan.

For sites without routine radiology reads:

1) Upon notification of a potential incidental finding from DPACC that was not previously noticed, the site should treat it as if their own staff had identified the incidental finding and follow their own institutional procedure.
2) Then, the site should document the outcome of that institutional procedure in the REDCap/RPMS “MRI Incidental Findings” form for the participant’s scanning session, regardless of whether or not the finding was deemed clinically significant or not.

For sites with routine radiology reads as part of the project:

1) Any radiologist recommendation for clinical follow-up should trigger completion of the REDCap/RPMS “MRI Incidental Findings” form, regardless of whether the DPACC has previously sent a notification. Please also let DPACC know via email.
2) Any notification from the DPACC of a potential incidental finding should trigger completion of the “MRI Incidental Findings” form, regardless of whether the site radiologist recommended clinical follow-up.

XII. DICOM export and upload

1. Any session that collects more than just the localizers and DistortionMap scans should upload that data as DICOMs to the appropriate network server (Yale XNAT for ProNET, Mediaflux for PRESCIENT), using the appropriate data transfer SOP.
2. When exporting from the scanner, do not use any vendor-implemented 'Anonymization', which may remove necessary/expected DICOM fields.
3. For Siemens sites on the **XA software platform**:
    a. **Do NOT export immediately after the conclusion of the final scan in the session** because it can take several minutes for the images to get stored/indexed properly in the scanner database. *Exporting too soon on XA systems may result in incomplete export of the final scan.* To be safe, check the file count of the final scan in the session in the Patient Browser or Export window prior to exporting to ensure that the count is as expected for that scan.
    b. DICOMs should be exported using the "**Enhanced DICOM**" format, to reduce the number of DICOMs generated. If exporting to "File System" (e.g, USB disk) you should use the "Image Conversion = Enhanced" option (which should be the default). If exporting to "Network" (e.g., local PACS or XNAT instance), the DICOM node itself needs to be configured properly on the scanner to export in Enhanced DICOM format. The Imaging Core can assist with the appropriate settings, if necessary.
4. As a sanity check prior to uploading, ensure that the total number of DICOMs is consistent with what you would expect for that session, to avoid uploading incomplete sessions. The expected DICOM counts for a complete session, with no aborted or reacquired scans is:
    a. Siemens, Prisma: 2519 for VE11; 1548 for XA30 (Enhanced DICOM format)
    b. Siemens, non-Prisma: 2469 (VE11)
    c. GE, MR750: 103622
    d. Philips, Achieva: 103469

XIII. Error Prevention Measures and Internal AMP SCZ Auditing

To reduce errors, the following apply:

1. Site personnel that participate in the MRI data collection MUST be trained and approved by the Imaging Core representative or by the designated site staff.
2. Two approved site personnel must be present at all times during the scan. One person will be tasked to operate the scanner, the second person is tasked on assuring quality by making sure protocol is followed, by visually inspecting the images in real-time (or shortly after acquisition), and by documenting events in the online MRI Run Sheet. *It is expected that all acquisitions are reviewed at the scanner prior to the conclusion of the imaging session. This is critical for QC and assessment of whether certain scans need to be reacquired.*
3. A printed version of this SOP and the accompanying imaging SOPs should be readily available to the site personnel during the scan.
4. During the site training the Imaging Core and the site personnel will strive to identify additional site specific issues, and the Imaging Core will work with each site to generate a site specific "Cheat Sheet" as necessary that includes highlights of the scanning procedures and guidance/resolutions for any site specific issues that will be identified.

Internal audits of the procedures in this SOP are required to include the following steps:

1. Review two randomly-selected MRI Run Sheets. Verify that all required fields have been completed properly.
2. Observe scan sessions without advance warning, to check for adherence to the SOPs and consistency of implementation between operators.
3. Review the training steps performed for each operator.
4. Discuss with operators which aspects of procedure they find confusing or difficult to follow as stated in the SOPs. Report possible SOP amendments to remedy the confusion to Imaging Core, or retrain operators as necessary.

XIV. Document Control

Document location: Paper copies are valid only on the day they are printed. Refer to the author if you are in any doubt about the accuracy of any document(s).

Document approval: This SOP requires the approval of the responsible investigator, as do any changes thereto.

This SOP has been approved by: Drs. Ofer Pasternak and Michael Harms

XV. Change Log

Version	Date	Summary of Changes
1.0	2021.09.24	- First version distributed to AMP SCZ consortium members.
1.1	NA	- NA (skipped this version number).
1.2	2024.09.21	- Moved several sections from the Siemens-specific SOP to this general MRI Acquisition SOP, since they were appropriate/relevant for all platforms (i.e., "Before the scan session", "Participant Registration", "Imaging Protocol", and "Rescan procedures and unscheduled breaks"). - Clarified expectations regarding training in the presence of staff turnover. - Added information on handling of dental appliances. - Added section on "Documentation". - Added section on "Quality Control (QC)". - Added section on "MRI Incidental Findings". - Added section on "DICOM export and upload". - Various minor edits in preparation for public release.