MRI Procedure Manual

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Sponsor Signature Page

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Table of Contents

1. Overview

The purpose of this manual is to offer comprehensive guidance and establish standardized procedures for imaging in this clinical trial. These standardized procedures are designed to ensure the consistency, accuracy, and reliability of the acquired imaging, thereby supporting the trial's overall objectives and maintaining data integrity.

2. Parkinson's Progression Markers Initiative (PPMI)

The Parkinson Progression Marker Initiative (PPMI) is a longitudinal, observational, multicenter natural history study to assess progression of clinical features, digital outcomes, and imaging, biologic and genetic markers of Parkinson's disease (PD) progression in study participants with manifest PD, prodromal PD, and healthy controls. The overall goal of PPMI is to identify markers of disease progression for use in clinical trials of therapies to reduce progression of PD disability.

3. PPMI Imaging Core

The PPMI Imaging Core serves as the central hub for ensuring the consistency, quality, and integrity of the MRI image data collected during the trial. The Imaging Core's primary responsibilities include setup and approval of participating imaging centers, providing ongoing support, ensuring that all imaging data is collected and processed according to the trial guidelines, and performing a qualitative and quantitative assessment.

The Imaging Core monitors the quality of the imaging data submitted by each site. This includes performing quality control checks on the images received, providing feedback to sites, and requesting corrective actions if necessary. Together with the study sponsor, the Imaging Core will provide the necessary support to participating imaging centers to ensure optimal imaging results.

Imaging Core Lab responsibilities were transitioned from Invicro to XingImaging in November 2024. Imaging centers previously set up by Invicro must continue using the MRI scanner and parameters approved for use by Invicro. Consistent use of the same imaging system and parameters is crucial to maintaining the longitudinal integrity of trial results.

3.1 Imaging Core Contact Information

For questions related to image data submissions to the Imaging Core, technical imaging questions or questions related to queries received, please contact:

corelab.support@xingimaging.com

For questions related to the PPMI clinical protocol, please contact your clinical site study coordinator or other applicable clinical team contact.

4. Study Documents

A copy of this imaging manual and related documents will be available within the PPMI Electronic Trial Master File (eTMF), Florence, as well as the PPMI Site Management Core's (SMC) Learning Management System (LMS). Going forward, please consult both platforms to ensure you have the most current version of each manual and document.

Imaging Center Setup and Approval

5. Imaging Center Setup and Approval

5.1 Imaging Centers Previously Approved for PPMI Imaging by Invicro

All imaging centers that were previously setup and approved for imaging by the former imaging core lab, Invicro, are required to complete an abbreviated setup procedure. This process involves the following:

5.1.1 Imaging Center Personnel Training:

Training will be conducted through a web-based learning module. The training will focus on the image data transfer and query resolution procedures using XingImaging's image data management platform. Once the training is completed, imaging centers will be granted access to the image transfer platform and will be required to conduct a test transfer.

5.1.2 Test Image Transfer:

A test of the participant image transfer process using XingImaging's image data management platform is required for all sites. The test transfer should consist of DICOM image files, preferably from a recently acquired PPMI participant. If the data from a recently acquired PPMI participant is not available for transfer, a phantom may submitted.

Imaging centers previously setup by Invicro must continue using the MRI scanner and parameters approved for use by Invicro. Consistent use of the same imaging system and parameters is crucial to maintaining the longitudinal integrity of trial results.

Upon completion of the training and the successful receipt of the test transfer, the imaging core lab will notify imaging centers that they are approved to begin submitting PPMI participant imaging to the trial imaging data management platform.

5.2 Imaging Centers Not Previously Approved for PPMI Imaging

Imaging centers must undergo a qualification process before beginning to scan participants for the PPMI trial to ensure that they meet the trial's technical and operational standards. Centers who were not previously approved for PPMI imaging must complete the steps listed below.

5.2.1 Technical Questionnaire:

The first step in this process is the completion of a questionnaire which collects information on the site's imaging personnel, imaging equipment, including the make, model, and technical specifications of the MRI scanner, head coil, and processing software. This information is reviewed by the imaging core lab to assess the compatibility of the equipment with the trial's requirements.

5.2.2 Protocol Verification:

Following completion and review of the questionnaire, the imaging core lab will provide imaging centers with the acquisition parameters unique to their MRI scanner make and model for the purposes of building a dedicated protocol in the system for use in this trial. Once the protocol has been established, the imaging center will be requested to provide screen captures of the relevant acquisition and reconstruction screens to the imaging core lab for review.

5.2.3 Phantom Acquisition:

As part of the imaging core lab's setup process, each imaging center will need to perform a phantom acquisition. This submission helps assess scanner performance, ensures that a standardized protocol has been correctly implemented, and provides a baseline for evaluating

future study participant scans. Instructions for performing the phantom acquisition will be provided in a separate document.

5.2.4 Imaging Center Personnel Training:

Training will be conducted through a web-based learning module. The imaging core lab will provide user-specific accounts to the relevant clinical and imaging staff, granting them access to the training system. The training will cover the overall study objectives, the imaging schedule, the imaging procedure and guidelines to follow, as well as the procedures for image data submission to XingImaging's image management application and query resolution.

At least one primary imaging staff member responsible for conducting study imaging must undergo training by the imaging core lab. The imaging center is responsible for ensuring that all additional personnel are trained by the primary staff member initially trained by the imaging core lab. All additional training activities must be documented, and a copy of this documentation should be sent to the referring clinical site(s). For any further assistance with training or questions, please contact the imaging core.

Imaging Schedule of Assessments
&
Participant Naming Convention

6. Imaging Schedule of Assessments

Table 1: Schedule of MRI Assessments

Scan	Healthy Control [a]	PD [a]	Prodromal [a]
Screening	X	X	X
Baseline Scan [b]	X [c]	X [c]	X [c]
Visit 04 (12 months) [d,e]	-	X	X
Visit 06 (24 months) [d]	-	X	X
Visit 10 (48 months) [d]	-	X	X
Visit 13 (72 months) [d]	-	X [f]	X
Visit 15 (96 months) [d]	-	-	X
Visit 17 (120 months) [d]	-	-	X
Withdrawal Visit [g]	-	X	X
New Clinical Diagnosis Visit [h]	-	X	X

[a] Cohorts include participants newly enrolled in PPMI Clinical. Newly enrolled participants in PPMI Clinical will start with the screening Visit.
[b] Baseline MRI imaging must occur within 60 days of the Screening Visit.
[c] **Do not collect at Baseline Visit if collected at Screening Visit.**
[d] MRI imaging will occur within ±45 days either side of the target visit date.
[e] Only for participants who consented to the Screening visit under Clinical protocol amendment 3.2 (Version 2.2 dated January 30, 2023).
[f] If the participant is beyond Year 6, conduct this activity at next annual visit.
[g] If a participant withdraws from the study and agrees to attend one more visit, follow the Clinical protocol Event Driven Modification of Scheduled Visits for withdrawal from study to determine if imaging should be completed.
[h] Follow the Clinical protocol Event Driven Modification of Scheduled Visits to determine if imaging should be completed.

7. Participant Naming Convention

Each participating site and study participant will receive a unique study-specific identification number. Both the site and participant numbers must be entered into image data management platform when transferring image files to the imaging core lab and must be used in all study documentation and communications with the imaging core lab.

- Site Numbers for this study consist of 3 digits.
- Participants moving from PPMI 001 to PPMI Clinical will retain their previously assigned 4 or 5-digit Subject ID.
- New participants enrolled in PPMI Clinical will be assigned a Subject ID up to 7-digits.

Sites should redact all protected health information (PHI) to protect the privacy of participants before submitting image data to the imaging core lab. This process involves redacting or removing any direct identifiers, such as names, addresses, contact details, or any other information that could be used to trace the identity of the participant. The image data management submission platform performs a secondary de-identification upon submission to the imaging core lab.

Data Submission to the Imaging Core, Query Management & Data Archival

8. Data Submission To The Imaging Core

Visit details and image files will be transferred to the imaging core lab through a web-based image management system. The DICOM image files will be uploaded directly into the application, while visit information will be entered directly into an electronic form within the system.

All acquired imaging must be transferred to the imaging core, preferably within 24 hours, but no later than 3 business days. All queries issued by the imaging core must be responded to within 5 business days.

The visit information and image series listed below are required to be available to complete the submission.

Instructions on use of the image management platform are provided in a separate manual which is available within the PPMI Electronic Trial Master File (eTMF), Florence, as well as the PPMI Site Management Core's Learning Management System (LMS).

8.1 Visit Information:

- Site and Subject ID
- Scan Date
- Visit Identifier
- Sequences Acquired
- Scan Comments: Please include information which may be helpful to the imaging core (e.g. participant positioning, parameter variations, etc.). Information provided may help avoid queries.
- Equipment Quality Assurance information

8.2 Image Files:

- DICOM files of each required image series

9. Query Management

The imaging core lab will perform a thorough quality control review of the received images, assessing them for adherence to the trial protocol and overall image quality. If any issues are identified, the imaging core lab will provide feedback to the imaging center through queries issued within XingImaging's image management platform and request corrective actions if necessary. This may include repeating the imaging procedure or implementing changes to the imaging process.

10. Data Archival

In accordance with Good Clinical Practice (GCP) guidelines (or regional regulations, whichever sets the higher standard), maintain an archive of all image data in a readable format, consistent with the format submitted to the imaging core.

Please contact the imaging core if your center has questions around meeting this data archival requirement.

MRI Visit Procedures
&
Imaging Equipment Information

11. MRI Visit Procedures

11.1 Participant Scheduling

The clinical site staff are responsible for scheduling the participant's MRI visit with the imaging center. Typically, the clinical site study coordinators are responsible for the scheduling of study-related activities. Effective communication between the clinical site and the imaging center is essential to timely scheduling in accord with the study visit windows.

11.2 Participant Preparation

Adhere to local participant preparation and safety guidelines for MRI. The responsible physician or a designated staff member at the MRI center will confirm the participant's ability to complete the MRI study.

11.3 MRI Imaging Protocol

The MRI protocol is designed to ensure consistent and high-quality images across all clinical sites. Adherence to the protocol is essential for the accurate assessment of the imaging data and the overall success of the trial.

Imaging Core Lab responsibilities were transitioned from Invicro to XingImaging in November 2024. Imaging centers previously set up by Invicro must continue using the MRI scanner and parameters approved for use by Invicro. The instructions included within this manual remain constant with prior PPMI imaging guidelines for continuity of the image acquisition. Consistent use of the same imaging system, procedures and parameters is crucial to maintaining the longitudinal integrity of trial results.

The exact parameters for each MRI sequence may differ slightly by site and will be decided as part of site set up by the Imaging Core.

11.3.1 Participant Positioning

- The participant should be positioned supine on the imaging table, with their head secured to minimize movement during the scan.
- A comfortable and stable positioning system should be used to ensure that the participant remains still throughout the imaging procedure. Motion artifacts can significantly degrade image quality and may require a repeat scan.
- The participant should be informed of the importance of avoiding voluntary head movements, asked to actively cooperate, and immobilized according to standard brain imaging procedures.
- The participant should be informed about the total acquisition time and positioned for maximum comfort using proper back support and support under the knees.
- There should be no left-right or ear-to-shoulder head tilt, and the participant's neck should not be hyper- extended or retracted.
- The participant's head should be centered in the head coil using the nasion (see example to the right) as an anatomical landmark. Ensure the participant is high enough in the coil to avoid loss of signal at the inferior aspects of the brain.

Parallel imaging can be used to shorten scan time. Be sure to follow the manufacturer's guidelines when implementing this technique.

Please inspect all scans for motion artifacts and other image distortions. According to your internal standards, repeat the sequences if necessary to achieve high-quality images suitable for analysis. Imaging centers may be required to redo scans if significant movement is detected during quality control review.

11.3.2 T1 3D Volumetric Sequence

To obtain precise quantitative measurements of brain structures and identify structural abnormalities, a high-resolution T1-weighted, 3D volumetric sequence (such as MP-RAGE or IR-FSPGR) will be acquired. The required parameters can be found in Table 2.

Positioning and Sequence Instructions:

- **Required Anatomical Coverage:** The field of view (FOV) should capture the full brain anatomy, including the vertex, cerebellum, and pons.
- **Slice Orientation:** Oblique sagittal, aligned with the longitudinal fissure based on both the axial and coronal localizers.

Table 2: T1 3D Volumetric Sequence Parameters

T1-weighted, 3D volumetric sequence (e.g. MP-RAGE, IR-FSPGR)	
Series Description	3D T1-weighted
Plane	Sagittal
Slice thickness (mm)	1.0 (slice thickness must remain consistent across timepoints)
Number of slices	192 (Please adjust slice thickness up to 1.2 mm to cover brain, if absolutely necessary. Please do not adjust the number of slices)
Voxel size (mm)	1.0*1.0 mm in plane resolution
Phase encode dir.	Anterior-Posterior (AP)
Matrix	256 x 256 (the use of interpolation, zero-filling or a ZIP factor is not permitted)
TR/TE/FA/other parameters	Will be defined by the imaging core according to the scanner
FOV	256 mm (full FOV required, no rectangular FOV)
Scan Time	~ 7 minutes

11.3.3 Resting State Functional MRI (rsfMRI) Sequence

Resting state functional MRI scans will be acquired to investigate functional connectivity within various brain regions. Refer to Table 3 for the imaging parameters used in both the initial and repeat resting-state fMRI sequences.

The imaging core lab will collaborate with the imaging center to determine the suitable sequences based on the scanner and software capabilities.

Positioning and Sequence Instructions:

- **Required Anatomical Coverage:** Ensure that one slice extends above the vertex. Use the remaining slices to cover the entire brain and as much of the cerebellum as possible. Center the slices in the axial plane to avoid aliasing in the anterior-posterior direction.

- **Slice Orientation:** Align slices along the anterior commissure-posterior commissure (AC-PC) plane.
- **Participant Instructions:** Instruct the participant to keep their eyes open throughout the scan and the importance of doing so. They should guided to concentrate on a fixed point. Immediately following the scan, confirm with the participant that their eyes remained open and they stayed awake. Ensure that no audio or video is played during the procedure.
- **Initial and Repeat rsfMRI Sequences:** Two Axial Resting State fMRI (BOLD) sequences must be acquired. The initial sequence, and a repeat sequence with the reverse phase encode direction to correct for distortion. The repeat scan includes a reversed phase encoding direction and an updated measurement count set to "10," while all other parameters should remain unchanged.

Table 3: Multiband Resting State fMRI Sequence Parameters

	Multiband 2D Gradient-echo T2*-weighted EPI	**Multiband REPEAT 2D Gradient-echo T2*-weighted EPI**
Series Description	rsfMRI_PA	rsfMRI_AP
Plane	Axial Oblique, plane parallel to AC-PC line	Axial Oblique, plane parallel to AC-PC line
Slice thickness (mm)	3.0 with no gap	3.0 with no gap
Number of Slices	52	52
Phase encode dir.	P >> A	A >> P
Matrix	66x66 (target voxel size 3.045x3.045mm)	66x66 (target voxel size 3.045x3.045mm)
FOV	201 x 201 mm	201 x 201 mm
Repetition Time (ms)	1000	1000
Echo Time (ms)	30	30
Flip angle	58	58
Slice order	Interleaved	Interleaved
Number of measurements	600	10
In-plane acceleration	1 (no acceleration in-plane)	1 (no acceleration in-plane)
Through slice acceleration	4 (Multiband/Hyperband factor)	4 (Multiband/Hyperband factor)
Instructions	Keep the eyes open and remain still	Keep the eyes open and remain still
Scan Time	~ 10 minutes	~ 25 seconds
Distortion Correction	Disabled	Disabled

Intensity correction filters	Enabled (Prescan Normalise, SCIC or PURE, CLEAR)	Enabled (Prescan Normalise, SCIC or PURE, CLEAR)

Specific parameters for each sequence may vary slightly depending on the site and will be determined during site setup. Alternative sequence parameters for scanners without access to MB/SMS sequences are provided in Appendix 1 and/or Table 7.

11.3.4 NM-MT Sequence

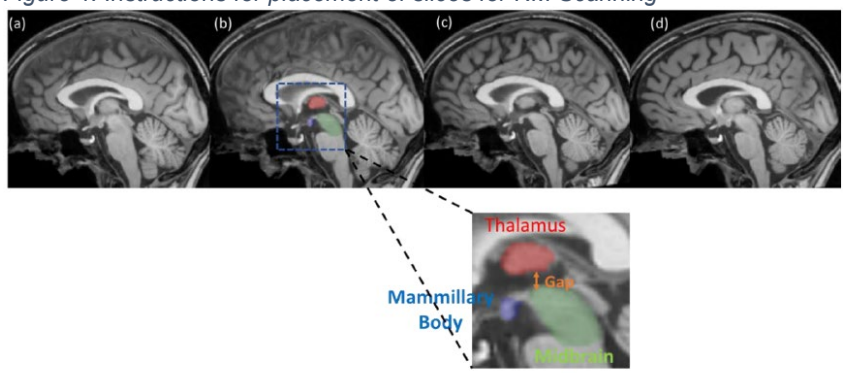
An MRI sequence specifically designed to be sensitive to neuromelanin (NM-MRI) will be performed, offering high contrast between the substantia nigra and the surrounding tissues. Required parameters are found in Table 4.

Positioning and Sequence Instructions:

- **Slice Positioning:** The scan will focus on select midbrain areas, making precise slice positioning essential. Refer to Figure 1 for detailed instructions on selecting the field of view (FOV) and Figure 2 for the final FOV placement and an example NM-MRI image.[1]
  - **Step 1**: Choose the sagittal plane that shows the widest gap between the thalamus and midbrain (either Figure 1b or 1c can be used for reference).
  - **Step 2**: Position the crosshair so that the coronal plane passes through the most anterior part of the midbrain, and the axial plane is placed 3 mm above the bottom of the third ventricle (as shown in the inset of Figure 1f). The axial plane (yellow line in Figure 1e) marks the superior boundary of the NM-MRI volume and should be aligned parallel to the AC-PC line.

[1] Wengler K, He X, Abi-Dargham A, Horga G. Reproducibility assessment of neuromelanin-sensitive magnetic resonance imaging protocols for region-of-interest and voxelwise analyses. *Neuroimage.* 2020;208:116457.

Figure 1: Instructions for placement of slices for NM Scanning



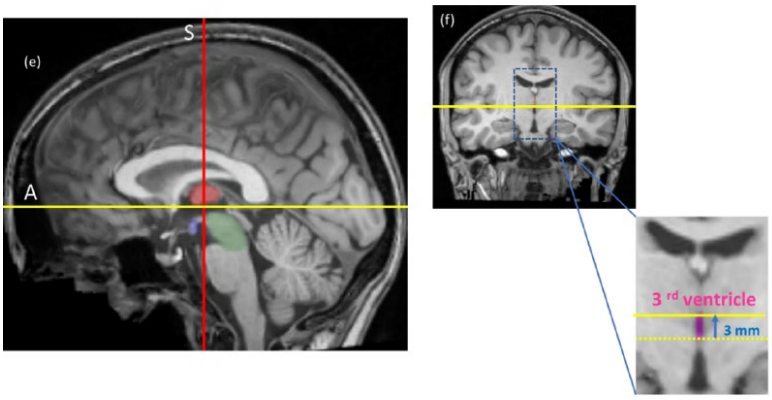
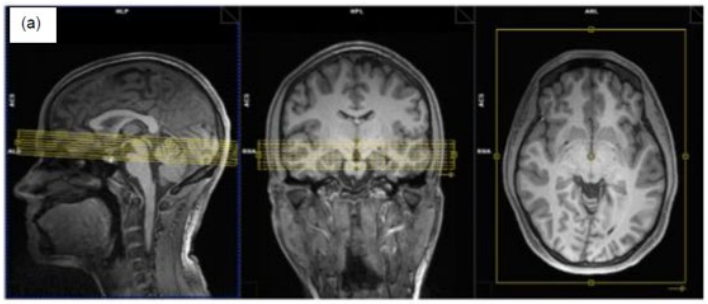
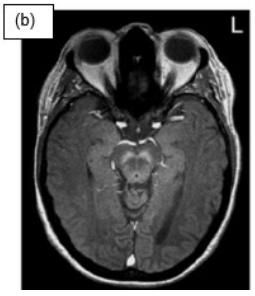


Figure 2: Final FOV placement (a) and Sample slice through the substantia nigra (b) (bright tissue in the midbrain (Chen et al. 2014)[2]





[2] Chen X, Huddleston DE, Langley J, et al. Simultaneous imaging of locus coeruleus and substantia nigra with a quantitative neuromelanin MRI approach. *Magn Reson Imaging.* 2014;32(10):1301-1306.

Table 4: NM-MT Sequence

2D Gradient recalled echo with MT preparation	
Series Description	2D GRE-MT
Plane	Oblique, follow instructions
Slice thickness (mm)	1.5 mm
Number of slices	16
Phase encode dir.	Right-Left (RL)
Matrix	440x440
FOV (mm)	220x220
Voxel Size (mm)	0.5 x 0.5 x 1.5
Repetition Time (ms)	~ 465 ms
TE	Minimum (< 5 ms)
Flip angle	40
MT Pulse FA	300°
MT offset Frequency	1.5 kHz (3.0 T)
MT pulse duration	10 ms
Measurements	5
Scan Time	~ 10 minutes
Receive Band Width	<500 Hz/Pixel

11.3.5 Diffusion Tensor Imaging (DTI) Sequence

Diffusion Tensor Imaging (DTI) will be acquired to study brain white matter integrity and connectivity. Refer to Table 5 for the required imaging parameters for the DTI sequences.

The imaging core will collaborate with the imaging center to determine the suitable sequences based on the scanner and software capabilities.

Positioning and Sequence Instructions:

- **Required Anatomical Coverage:** The slices should cover the brain from the vertex to the base of the cerebellum.
- **Participant Instructions:** Instruct the participant to stay completely still during the entire scan.
- **Initial and Repeat DTI Sequences:** To correct for susceptibility-induced distortions, two sequences with reversed phase encoding directions must be acquired. The number of

sequences will be determined by the type of sequence, the number of b-values, directions, and phase encoding directions, while all other parameters should remain unchanged.

Table 5: Multi-shell Diffusion Tenson Imaging (DTI)

Multiband 2D Diffusion-weighted EPI	
Series Description*	DTI_B0_PA; DTI_revB0_AP; DTI_B700_64dir_PA; DTI_B1000_64dir_PA; DTI_B2000_64dir_PA
Plane	Straight Axial
Slice thickness (mm)	2.0 with no gap
Number of Slices	72
Phase encode dir.	P >> A (b0 images to be acquired both P/A and A/P directions)
Matrix	116x116** (target voxel size 1.98x1.98mm)
FOV	230x230 mm
Repetition Time (ms)	~3800 (minimum allowed)
Echo Time (ms)	~90-100
In-plane acceleration	1 (no acceleration in-plane)
Through slice acceleration	3 (Multiband/Hyperband factor)
Flip angle	90
Fat Suppression	on
Slice order	Interleaved
Number of directions	64 per shell
B-Values	0, 700, 1000, 2000 s/mm2 ***
Instructions	Keep still
Distortion Correction	Disabled
Intensity correction filter	Enabled (Prescan Normalise, SCIC or PURE, CLEAR)
Note: *Phantoms and participant study scans will use the parameters detailed in this table.* ** Scan series description will vary dependent on sequence type, number of b-values, directions and phase encode direction. Additional guidance to be provided.* ***On GE systems, to prevent interpolation for 116x116 matrix, set USER CVs : rhrcyres = 116, rhrcxres=116, rhimsize=116* ****number of b-values to be acquired will be dependent on scanner capability. Multiple b0 images to be acquired. Additional guidance on order of sequences to be provided.*	

Specific parameters for each sequence may vary slightly depending on the site and will be determined during site setup. Alternative sequence parameters for scanners without access to MB/SMS sequences are provided in Appendix 1 and/or Table 8.

11.3.6 3D T2 FLAIR Sequence

A high-resolution 3D T2 FLAIR sequence will be acquired to evaluate white matter disease and other pathologies. Required parameters are provided in Table 6.

Positioning and Sequence Instructions:

- **Required Anatomical Coverage:** The field of view (FOV) should capture the full brain anatomy, including the vertex, cerebellum, and pons.
- **Slice Orientation:** Oblique sagittal, aligned with the longitudinal fissure based on both the axial and coronal localizers.

Table 6: 3D T2 FLAIR Sequence

3D T2 FLAIR Sequence	
Series Description	3D T2 FLAIR
Plane	Sagittal
Slice thickness (mm)	1.0 – 1.2 (slice thickness must remain consistent)
Number of slices	192 (please adjust slice thickness up to 1.2 mm to cover brain, not the number of slices)
Voxel size (mm)	1.0*1.0 mm in plane resolution
Phase encode dir.	Anterior-Posterior (AP)
Matrix	256 x 256 (the use of interpolation, zero-filling or a ZIP factor is not permitted)
TR/TE/FA/other parameters	Will be defined by the imaging core lab according to the scanner
FOV	256 mm (full FOV required, no rectangular FOV)
Scan Time	~ 7 minutes
Note: *Phantoms and participant study scans will use the parameters detailed in this table.*	

11.4 MRI Imaging Center Quality Control

Immediately following image acquisition, a quality control check should be performed by the technologist to assess the images for motion artifacts, correct positioning, and overall image quality. If any issues are identified, the scan may need to be repeated.

12. Imaging Equipment

12.1 Approved Equipment

The quality of the imaging data acquired in this clinical trial relies heavily on the use of high-performance, well-maintained imaging equipment. Only equipment that has been reviewed and approved by the imaging core lab may be used for participant imaging in the trial. The primary piece of equipment is the MRI scanner and head coil, which must be capable of producing high-resolution images with minimal artifacts. A 3 Tesla magnet is required for this trial.

The imaging center must ensure that all equipment is in good working order and is properly calibrated according to the manufacturer's specifications.

Any deviation from the approved equipment must be justified and pre-approved by the imaging core lab.

12.2 Equipment Changes

It is crucial that any changes to the imaging equipment used in the trial be reported to the imaging core lab immediately. Changes could include upgrades to the MRI hardware or software, replacement of key components, or the introduction of new ancillary equipment. Even minor changes can impact the consistency and quality of the imaging data, so they must be carefully evaluated by the imaging core lab.

If an imaging center plans to upgrade or replace its MRI scanner, it must notify the imaging core lab before making the change. The imaging core lab will assess whether the new equipment is compatible with the trial's protocols and whether requalification is necessary. The imaging center may be required to perform a new phantom scan and submit the images for review to ensure that the new equipment meets the trial's quality standards.

In cases where an imaging center needs to make an urgent equipment change due to unforeseen circumstances, such as equipment failure, the site must contact the imaging core lab as soon as possible.

12.3 Equipment Maintenance and Calibration

Proper maintenance and calibration of imaging equipment are essential to ensure consistent image quality throughout the trial. Imaging centers are responsible for implementing a regular maintenance schedule for their MRI scanner and associated equipment, following the manufacturer's recommendations and any additional guidelines provided by the imaging core lab.

Calibration of the MRI scanner system components should be performed regularly, with particular attention to the magnet, gradient coils, and RF systems. Calibration should be documented in a logbook or electronic record, and these records must be made available to the imaging core lab upon request. Any discrepancies or issues identified during calibration must be addressed promptly, and corrective actions must be documented.

In addition to routine maintenance and calibration, the imaging center should perform regular quality control checks, such as image quality through use of a phantom (uniformity, spatial resolution, signal to noise, etc.), safety, geometric accuracy, RF coil performance checks. These checks help ensure that the equipment is functioning optimally and that any potential issues are

identified and corrected early. The imaging core lab may request periodic submission of quality control data to verify that the site is maintaining the required standards.

13. History of Change

Version History		
Version Number	Version Date	Description of Change
1.0	2025-Jan-22	Original

14. Appendix 1: Alternate rsfMRI and DTI Sequence Parameters

14.1.1 Alternate rsfMRI Sequence Parameters

The parameters provided below may be utilized for MRI facilities without access to multiband (MB) or simultaneous multislice (SMS) imaging capabilities. Use of these alternate parameters must be approved by the imaging core lab.

Table 7: Alternate rsfMRI Sequence Parameters

	2D Gradient-echo T2*-weighted EPI	**REPEAT 2D Gradient-echo T2*-weighted EPI**
Series Description	rsfMRI_RL	rsfMRI_LR
Plane	Axial Oblique, plane parallel to AC-PC line	Axial Oblique, plane parallel to AC-PC line
Slice thickness (mm)	3.5 with no gap	3.5 with no gap
Number of Slices	~ 40	~ 40
Phase encode dir.	R >> L	L >> R
Matrix	64x64	64x64
FOV	224 x 224 mm	224 x 224 mm
Repetition Time (ms)	2500	2500
Echo Time (ms)	30	30
Flip angle	80	80
Slice order	Interleaved	Interleaved
Number of measurements	240	10
In-plane acceleration	GRAPPA or SENSE (factor of 2)	GRAPPA or SENSE (factor of 2)
Instructions	Keep the eyes open and remain still	Keep the eyes open and remain still
Scan Time	~ 10 minutes	~30 seconds

14.1.2 Alternate DTI Sequence Parameters

Table 8: Alternate DTI Sequence Parameters

Two sequences with reversed phase encoding direction must be acquired in full to correct for susceptibility induced distortions.

2D Diffusion-weighted EPI	
Series Description	DTI_RL (and DTI_LR for the repeated scan with reverse PE)
Plane	Straight Axial
Slice thickness (mm)	2.0 with no gap
Number of Slices	~ 80
Phase encode dir.	R >> L (L>>R for repeated scan)
Matrix	128x128*
FOV	256x256 mm
Repetition Time (ms)	~10000
Echo Time (ms)	~80
Flip angle	90
Slice order	Interleaved
Number of directions	32
B-VALUE	0 and 1000 s/mm2 (B=0 images interleaved throughout if possible in product sequence)
Instructions	Keep still
Scan Time	~ 8 minutes
Note: **On GE systems reconstructed final images will be 256x256 – to prevent interpolation for 128x128 matrix, set USER CVs: rhrcyres = 128, rhrcxres=128, rhimsize=128*	