



ReD-Lat
Multi-Partner Consortium
to Expand Dementia
Research in Latin America

MRI Collection Manual

Version 1.0
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Contents

Contacts for ReDLat	3
Study Aims	3
Site-Specific Parameters	3
Participant Pre-Scan Procedures	4
Participant Pre-screening	4
Participant Safety and Monitoring	4
Participant Positioning	5
Participant Scan Protocol	5
Participant Scan Procedures	6
ReDLat MRI Tracking Form in REDCap	6
Entering participant information into the scanner	6
Scan Discontinuation	6
Archive Procedures	6
Data Transfer	6
Quality Control	6
Visual Checking	6
Data Transfer Guide	8
Visual Scales	8

Contacts for ReDLat

For any questions related to MRI acquisition or data transfer, please email redlat.coordinacion@gmail.com

Study Aims

To identify the unique genetic and social determinants of health/socio-economic status (SDH/SES) factors that drive AD and FTD presentation in Latin American Countries (LAC) relative to the US, including risk factors, cognitive profiles, and brain imaging. We will establish a first-in-class cohort anchored in at least six LAC (currently: Argentina, Chile, Colombia, Brazil, Mexico, and Peru), compared to US samples (totaling > 4200 participants, including 2100 controls, 1050 AD participants, and 1050 FTDs participants). We will also assess novel families across LAC via the Latin America and Caribbean consortium on Dementia (LAC-CD). In addition to the strategy based on patients with sporadic presentations tested for genetic risks (risk scores), the project will also support recruitment of AD and FTD families with an autosomal dominant-like presentation from the LAC-CD. We will couple standardized clinical assessments with innovative analytical techniques to account for heterogeneity in these diverse populations.

General hypothesis: There are unique risk factors for AD and FTD in LAC (e.g., genetic risk factors enriched in LAC populations; underlying cognitive and neural vulnerability due to SES/SDH) compared to US populations. Our plan to recruit large numbers of controls and patients across these diverse populations will provide opportunities to identify new genetic and SES/SDH risks for AD and FTD. In addition, the machine learning strategies will reduce the impact of heterogeneity and will allow us to refine the accuracy of association studies.

Site-Specific Parameters

Each site will follow the standard acquisition parameters for their center. These parameters will be shared with the coordinating center prior to beginning enrollment and any changes to the parameters over the course of the study should be sent to redlat.coordinacion@gmail.com.

Every effort should be made to collect every scan on the same scanner.

COUNTRY	SITE	IMAGING CONTACT	SCANNER MODEL
Argentina	Ibañez	Ignacio Brusco	3 T Philips
Argentina	Brusco	Ignacio Brusco	3 T Philips
Argentina	Bruno	Luciana Vitta	1.5T GE Signa Explorer
Brazil	Takada	Douglas Mendes	3T Philips Achieva
Chile	Behrens	Lizzie Behrens	3T Philips Ingenia
Chile	Slachevsky	Nicolas Crossley	3T Philips Ingenia
Colombia	Matallana	Pablo Reyes	3T Philips Achieva
Colombia	Cardona	Sebastián Grisales	3T Philips Achieva

Colombia	Lopera	Natalia Trujillo	
Mexico	Sosa	Ana Luisa Sosa Francisco Flores	3T Siemens Skyra
Mexico	Avila-Funes	Griselda Teresa Romero Sanchez	1.5T Philips Achieva
Peru	Custodio	Maria Elizabeth Moron	3T Siemens Skyra
US	Miller	Amy Wolf	3T Siemens Prisma Fit

Participant Pre-Scan Procedures

Participant Pre-screening

All participants should have been screened by the study coordinator for standard MRI contraindications. However, participants must be screened for MRI contraindications immediately before the MRI scan using the local standard protocol. Contraindications include, but are not limited to:

- The presence of non-removable ferrous metal objects
- Aneurysm clips
- Pacemakers
- Other contraindications such as defibrillators, etc.

In order to minimize the chance that a participant will ask to discontinue the scan, sites may wish to share a brief video before the visit that illustrates the purpose, duration, restrictions, and possible discomforts. If requested, relatives may also be allowed to join the participant in the scanner room. Sedation can be used in rare cases if deemed appropriate by the site clinician and if approved by the local ethics committee. If sedation is used, it should be noted in the **ReDLat MRI Tracking Form** in REDCap. Sedation should not be administered prior to any cognitive testing.

Participant Safety and Monitoring

- All sites should follow the standard consent protocols as approved by the local IRB.
- Explain the scan procedure to the participant so that they know what to expect during the MRI.
- Provide the participant with the opportunity to use the restroom before the scan begins.
- Use universal MRI safety precautions. Make sure that participants does not have any large ferrous metal on or inside of him/her such as shrapnel, a metal fragment in the eye, aneurysm clips, ear implants, spinal nerve stimulators, permanent makeup, or a pacemaker. Make sure that all loose metal objects are removed.
- Participants are allowed to take their medications on the day of the scan. However, sedatives will interfere with the functional MRI and should be avoided if possible. If a participant has a prescription for a sedative (such as Valium) and this medication cannot

feasibly be withheld, the sedation (agent, dose, time administered) should be noted on the **ReDLat MRI Tracking Form** in REDCap.

- Offer the participant hearing protection.
- Use standard local practice for monitoring the participant during the scan. These may include MRI safe devices to monitor pulse and O2 levels.

Participant Positioning

Proper positioning is crucial for successful comparison of MRI exams. Therefore, it is important that each participant is positioned in the same manner for every MRI exam. Follow the procedures below for positioning the participant in the head coil:

- Place clean sheet on scanner table and coil cradle.
- Besides standard room exclusions ensure the participant has removed their dentures as well as any hair clips, combs, earrings, necklaces, etc.
- Remove all upper body clothing with metallic trim, such as zippers, buttons or embroideries that may cause artifacts in the MRI images.
- Provide each participant with ear protection.
- Position the participant so their head and neck are relaxed, but without rotation in either plane. Proper placement in the head coil is crucial because scans are acquired straight, not in an oblique orientation. The participant should also be well supported in the head coil to minimize movement. Motion artifacts may result in data that is not usable.
- Support under the back and/or legs can help to decrease strain on the knees and back as well as assisting in the stabilization of motion in the lower body.
- Once participant has been positioned, place sponges along the sides of head and a Velcro strap across forehead (if available) for stabilizing support and reduction of motion.
- Align the centering crosshairs directly between the eyebrows.
- Center the head coil over the participant's head, making sure the participant is high enough in the coil to prevent signal loss at the inferior aspect of the brain.
- Offer the participant a panic button in case of emergencies or claustrophobia if common local practice at your facility (for example, a squeeze ball alarm.)
- Remind participant to hold as still as possible and advance participant to the iso-center of the scanning bore.
- If a deviation from these instructions is required to accommodate a participant, this should be noted on the **ReDLat MRI Tracking Form** in REDCap.

Participant Scan Protocol

Core ReDLat Scan Sequences:

1. 3 Plane - T1
2. 2D Axial or 3D FLAIR
3. Resting-state fMRI (eyes open)

Additional ReDLat Scan Sequences (to be collected whenever possible, but not required):

1. 2D Axial or 3D SWI
2. 3D ASL

3. DTI

	suggested voxel size (mm)	Suggested parameters (ms) (may vary among scanners)	sequence duration (min)
3D-T1	1 x 1 x 1 mm	vary depending on scanner brand	6
2D axial or 3D FLAIR	1 x 1 x 1 mm	vary depending on scanner brand	6
rs-fMRI	2.5 - 3 mm isotropic	TR = 2500 ms, TE30 ms	10
2D axial or 3D SWI	2D: 3-5 mm and 2 x 2 mm. 3D: 1mm isotropic	vary depending on scanner brand	5
3D-ASL	1.9 x 1.9 x 4	TE= 10.5 TR = 4885 PLDelay = 2000	4
DTI	2 x 2 x 2	TE= 71 TR = 3300 , 16 directions	7
Total Time (min)			38

Participant Scan Procedures

ReDLat MRI Tracking Form in REDCap

The **ReDLat MRI Tracking Form** in REDCap should be completed at the time of acquisition for every participant. Please be sure to indicate if each sequence has been completed and note any problems or modifications to the protocol in the appropriate sections. It may be helpful to keep a copy on site for the study records.

Entering participant information into the scanner

Although the scan header will be de-identified and rendered HIPAA compliant when data is transferred, it is preferred that you use the ReDLat participant naming convention when entering the information into the scanner. Patient name and Patient ID should match the ReDLat PIDN, with the format "XX#####". Instructions for PIDN generation can be found in the study manual. For centers where the scan is collected for clinical purposes and patient information must be entered at the time of collection, Patient Name and Patient ID should be replaced by the ReDLat PIDN following the radiologist's review of the image.

Scan Discontinuation

If the participant elects to discontinue the MRI because of discomfort every effort should be made to adjust the table, head coil, etc. and finish acquiring the scan. However, if the participant still does not want to complete the scan, then the MRI should be abandoned and noted as incomplete on the **ReDLat MRI Tracking Form** in REDCap. The comments section should include the reason the participant was unable to complete the MRI.

Archive Procedures

Every MRI scan must be archived at the local facility following standard practice.

Data Transfer

Each scan should be uploaded within 7 days of collection.

Quality Control

Visual Checking

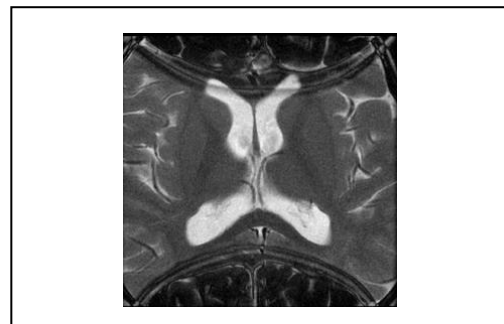
Before uploading data, each image should be visually inspected for quality:

- Was the whole brain captured?
- Was there significant movement?
- Any artifacts?

The FSL primer offers examples of artifacts and can be useful tool when inspecting for image quality (https://www.fmrib.ox.ac.uk/primers/intro_primer/ExBox1/IntroBox1.html). Overall image quality should be rated on a 0-4 scale and this value should be noted **ReDLat MRI Tracking Form** in REDCap.

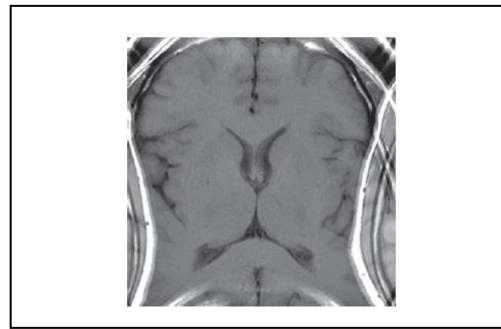
Image Quality Scale

- 0** An image with this score has substantial quality issues. There may be a large artifact or the FOV may not cover the entire brain.

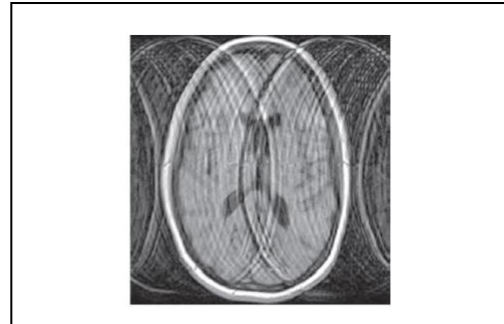


Aliasing (wrap-around) artefact generated due to incomplete FOV. Axial T2 weighted image (Case courtesy of Dr Usman Bashir, <https://radiopaedia.org/>). From the case <https://radiopaedia.org/cases/16491> rID: 16491).

Axial T1-weighted image showing wrap-around artifacts due to the smaller FOV (Morelli JN, Runge VM, Ai F, Attenberger U, Vu L, Schmeets SH, Nitz WR, Kirsch JE. An image-based approach to understanding the physics of MR artifacts. Radiographics. 2011 May-Jun;31(3):849-66. doi: 10.1148/rg.313105115. PMID: 21571661)

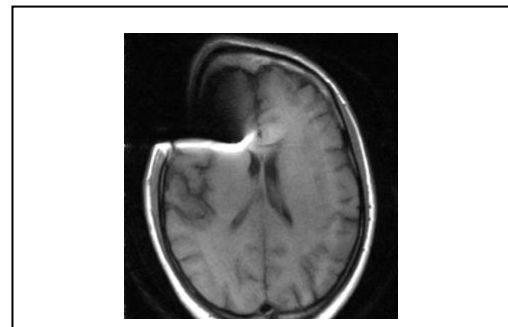


- 1 An image with this score has quality issues. There may be artifact or motion. There may be some wrapping of the image or other FOV issues.

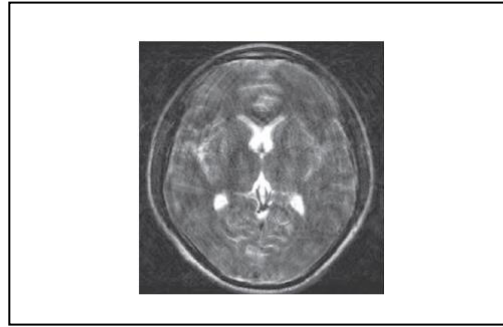


Axial T1-weighted image showing a significant ghosting artifact due to patient motion. FOV is complete. (Morelli JN, Runge VM, Ai F, Attenberger U, Vu L, Schmeets SH, Nitz WR, Kirsch JE. An image-based approach to understanding the physics of MR artifacts. Radiographics. 2011 May-Jun;31(3):849-66. doi: 10.1148/rg.313105115. PMID: 21571661).

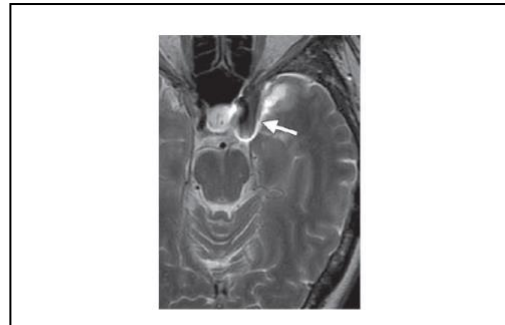
Significant magnetic susceptibility artefact in T1-weighted scan (Case courtesy of Dr Ayush Goel, [Radiopaedia.org](https://radiopaedia.org/)). From the case <https://radiopaedia.org/cases/22731> rID: 22731).



- 2** An image with this score does not have FOV issues, but may have some other quality concerns. There may be minor artifact or motion that would make research analysis challenging.

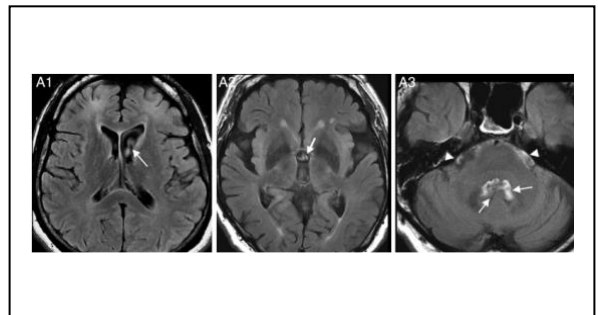


Axial T2-weighted image depict a ghosting artefact caused by patient motion (Morelli JN, Runge VM, Ai F, Attenberger U, Vu L, Schmeets SH, Nitz WR, Kirsch JE. An image-based approach to understanding the physics of MR artifacts. Radiographics. 2011 May-Jun;31(3):849-66. doi: 10.1148/rg.313105115. PMID: 21571661).



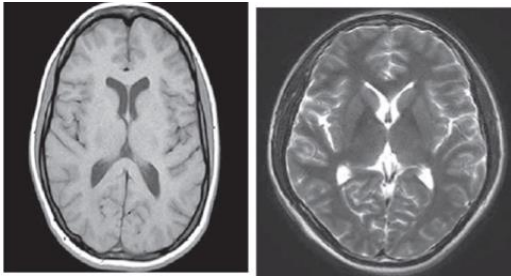
Axial T2-weighted image depict a small magnetic susceptibility artefact caused by an aneurysm clip (Morelli JN, Runge VM, Ai F, Attenberger U, Vu L, Schmeets SH, Nitz WR, Kirsch JE. An image-based approach to understanding the physics of MR artifacts. Radiographics. 2011 May-Jun;31(3):849-66. doi: 10.1148/rg.313105115. PMID: 21571661).

- 3** An image with this score may have minor artifact or motion issues, but is still usable for research purposes.



Axial FLAIR images depicting CSF artefacts (white arrows) Lummel N, Schoepf V, Burke M, Brueckmann H, Linn J. 3D fluid-attenuated inversion recovery imaging: reduced CSF artifacts and enhanced sensitivity and specificity for subarachnoid hemorrhage. AJNR Am J Neuroradiol. 2011 Dec;32(11):2054-60. doi: 10.3174/ajnr.A2682. Epub 2011 Sep 15. PMID: 21920855

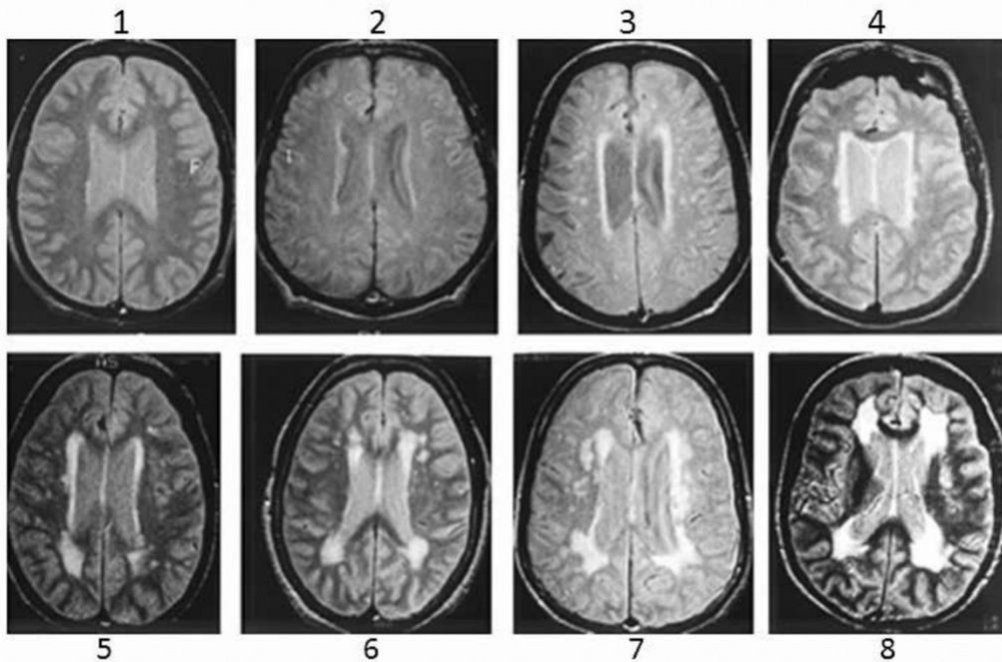
- 4** An image with this score has no artifact and no discernable motion. This is a high-quality image.



T1 (left) and T2-weighted (right) axial images

Visual Scales

Visual scales will be completed by trained specialists using the Cardiovascular Health Study scale.



Longstreth WT Jr, Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA, Enright PL, O'Leary D, Fried L. Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study. *Stroke*. 27(8):1274-82, 1996.

Grade 0: no white matter findings

Grade 1: discontinuous periventricular rim with minimal dots of subcortical disease

Grade 2: thin, continuous periventricular rim with a few patches of subcortical disease

Grade 3: thicker, continuous periventricular rim with scattered patches of subcortical disease

Grade 4: thicker, shaggier periventricular rim with mild subcortical disease, may have minimal confluent periventricular lesions

Grade 5: mild periventricular confluence surrounding the frontal and occipital horns

- Grade 6: moderate periventricular confluence surrounding the frontal and occipital horns
- Grade 7: periventricular confluence with moderate involvement of the centrum semiovale
- Grade 8: periventricular confluence involving most of the centrum semiovale
- Grade 9: findings more remarkable than grade 8

Instructions to convert images from DICOM to NifTI

Step 1. Download MRICroGL at <https://www.nitrc.org/projects/mricrogl/> selecting the version compatible with your OS (i.e., Windows, Linux, or macOS).

Step 2. Run the executable file on your installation folder.

Step 3. MRICroGL includes a simple graphical user interface for controlling dcm2nii. After launching MRICroGL, click on the Import tab, then click on convert **DICOMtoNifTI** menu item. The interface is shown in the figure below.

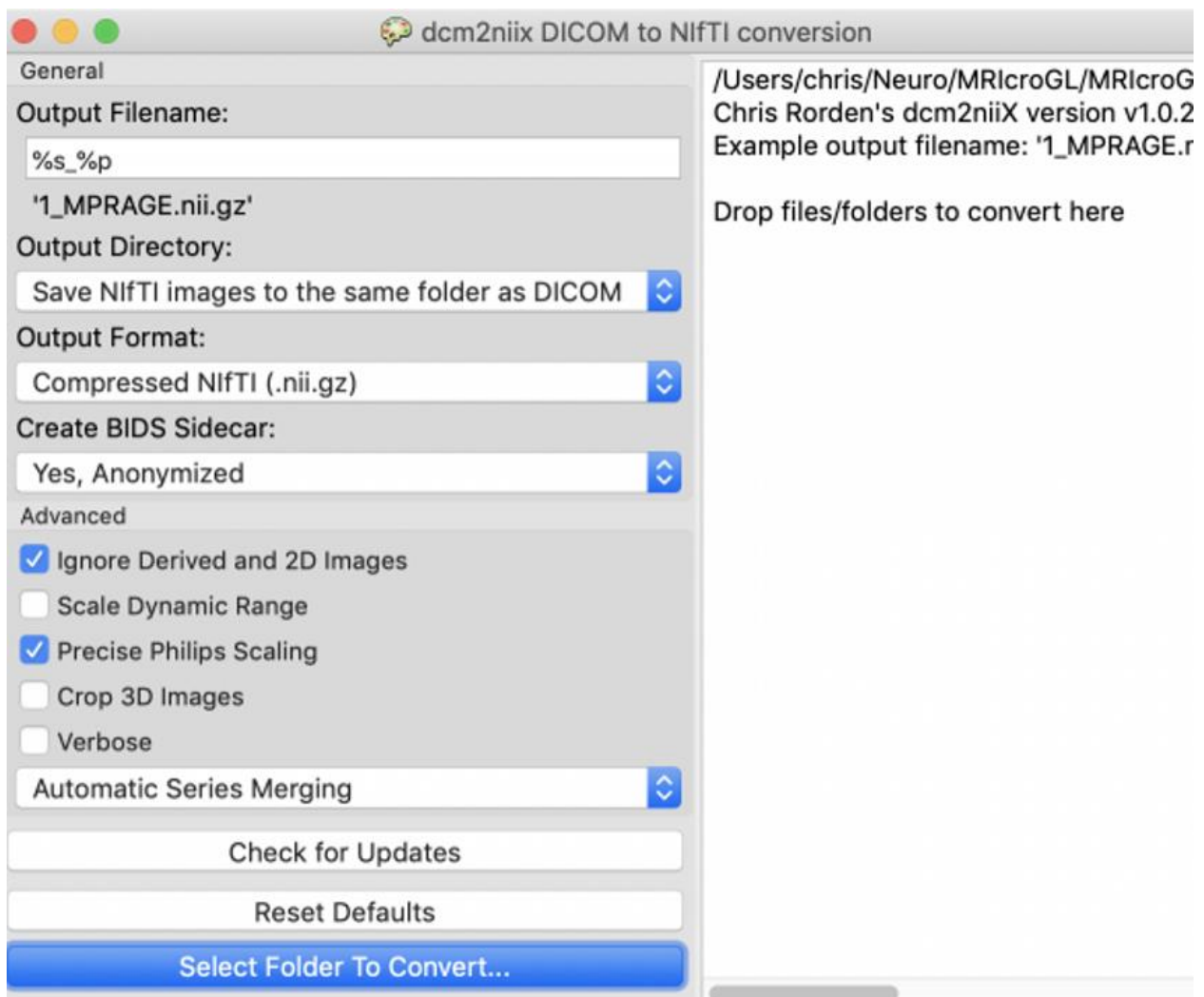


Figure 1. Graphical user interface of MRICroGL DICOM to nifti: The check box sets whether the output will be compressed (creating .nii.gz files) or uncompressed (creating .nii files). You can then specify the desired output filename. When you adjust the desired output name, the software will display an example for how your files will appear. You can also select whether you

want to save the output to a specific folder or whether the NIfTI images should be created in the same folder as the input DICOM files. The final step is to drag and drop the folder you wish to convert onto the application. Note that the interface always interactively shows you the command line, so that as you interact with the interface by selecting checkboxes you are creating a text command you can copy and paste into your favorite script.

Step 4. Select the options as see them in figure 1:

Output filename: Allows you to specify how the converted NIfTI files are named. If you specify "%s%p" for your first subject **sub1** - in this case the name of the series and the protocol number (as stored in the DICOM file) will become part of the file name. In this case the output files will be named **sub1fmri1.nii**.

Output format: Select compressed **nii.gz** to save space.

Create BIDS sidcar: The software will generate a Brain Imaging Data Structure file with the same name as the NIfTI image. This file is in the JSON text format, providing additional information about the scan that cannot be saved in the NIfTI header. Select **yes, Anonymized**.

Ignore Derived and 2D images: To not take into account images that will not be used.

Precise Philips scaling: This option only has an effect if your image includes both these scaling factors.

Automatic series merging: Merge similar series.

Brain Imaging Data Structure (BIDS)

The Brain Imaging Data Structure (BIDS) defines a format for the file names, folder structures and file types for neuroimaging data. While MRICroGL does create BIDS-compatible NIfTI and JSON files, it does not replicate the file names and folder hierarchy described by BIDS. You have to create the folder structure as shown below.

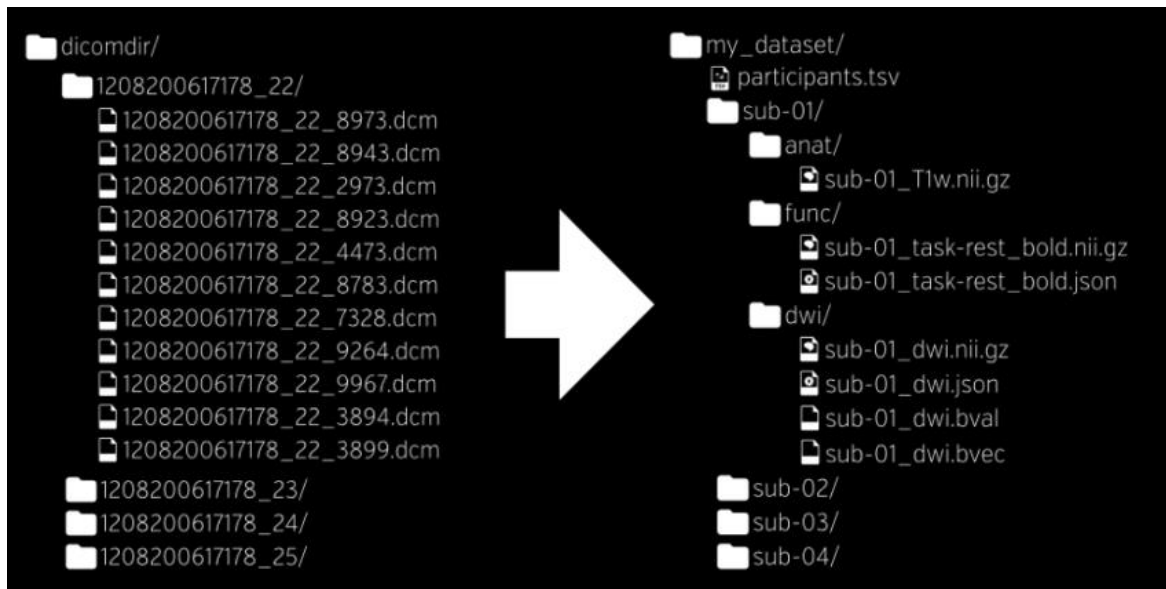


Figure 2. Example of a dicom to BIDS data structure conversion.

Use the example structure at the right of figure 2 to create your folders and subfolders.

Create a participants.tsv (tab-separated values) file to store subject's data such as local ID, ReDLat ID, folder name to be used (e.g., sub-1), demographics (sex, age, etc.), handedness, and neuropsychological outcomes (MoCA, IFS, etc.) in your main folder. You can use Excel and then save your spreadsheet as a .tsv file.

For each subject folder (sub-1, sub-2, sub-3) create three folders (anat, func, and dwi). You will copy the output generated after the conversion for each sequence, including the .json files and bval and bvecs in case of DTI.

- On anat you will put the anatomical series (T1, FLAIR, etc.) on nii.gz format.
- On func you will put the resting-state acquisition nii.gz file.
- On dwi you will put the DTI analysis (including the bval and bvec files).

Please make sure that your output resembles the example shown at figure 2 before uploading to the ReDLat database.