National Institutes of Health
National Institute of Neurological Disorders and Stroke
National Institute on Aging

MarkVCID2 Imaging Manual

Version 1.6.7, 2.27.25
MarkVCID Consortium

MarkVCID Imaging Biomarkers Subcommittee (MarkVCID1 co-chair Konstantinos Arfanakis, PhD and MarkVCID2 co-chair Prashanthi Vemuri, PhD) and Coordinating Center (Data Core Director / Subcommittee co-chair Karl Helmer, PhD and MarkVCID PI Steven M. Greenberg, MD, PhD).

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Contact Information

Contact Group	Topic	Contact email
MarkVCID Coordinating Center (CC) Imaging Team	Questions or concerns related to MRI imaging study procedures and protocol	markvciddata@mgh.harvard.edu Subject line: Imaging: <issue reference>
MarkVCID Data Management Core (DMC)	Questions or concerns related to data de-identification and transfer, Globus installation, and scan-session registration issues	markvciddata@mgh.harvard.edu Subject line: DMC: <issue reference>

1. General Instructions

The purpose of this manual is to provide detailed instructions for all aspects of MarkVCID study imaging data: acquisition, registration, de-identification, and transfer.

1.1 Record Keeping

Sites should log each MarkVCID participant imaging session. We suggest using the MarkVCID_Imaging_Session_Log_Template found in the Imaging Resources section of the Consortium Protocols & Resources page on the MarkVCID website (markvcid.org). This template can be used to store the participant ID, the registration ID for the dataset that is generated at the time of registration, and the scan date. This document should also be used to store the name and email address of the person performing the Fazekas evaluation and the date of that evaluation for each of the scan sessions.

1.2 MRI Scanner

All MarkVCID MRI scans must be acquired on the MRI scanner that was used in the site certification process. If a different MRI scanner is used, the scan will fail the quality control check and the site may be asked to rescan the participant on the approved scanner. Any change of scanner must be pre-approved by the MarkVCID Imaging Team. Please inform the MarkVCID Imaging Team of any planned changes in scanner hardware or software at least 4 weeks in advance so that re-certification can be performed with minimal interruption of participant scanning. If a site fails to perform the phantom scans and receive certification prior to a participant being scanned on the upgraded scanner, the DMC may not accept the participant scans.

1.3 Head Coil Selection

Sites generally have a range of head coils available for a study. Sites should select the coil with the largest number of channels that, in their experience, has comfortably fit a large majority of patients at their site. Sites should strive to use the same head coil for each participant in the study.

2. Site Certification for MRI Scanning

2.1 Contact Information

If you have any questions or concerns regarding MRI imaging, please contact the MarkVCID Coordinating Center Imaging Team. Questions can also be raised on the Imaging Subcommittee calls and through Imaging Subcommittee group emails where appropriate.

2.2 Overview

Prior to scanning any MarkVCID participants, the site must complete the MRI Scanner Certification procedure. In most cases, site MRI Scanner Certification will only involve scanning a phantom with the harmonized MarkVCID sequences. The procedure is:

- Implement the site-harmonized protocol on the MRI scanner
- Send a PDF of the protocol as implemented on the scanner to the CC Imaging Team using the email address in the Contact Information table above.
- Once approved by the CC Imaging Team, scan an MRI phantom using the approved protocol
- Transfer the phantom data to the CC Imaging Team using the Globus data transfer service
- If approved by the CC Imaging Team, the site is considered “certified” and will receive an official certification letter. If the protocol requires changes, this process will be repeated until the images and protocol are satisfactory.

2.3 MarkVCID Harmonized Imaging Protocol

Prior to scanning, a scanning protocol, harmonized across all the scanner manufacturers and models in the consortium, will be constructed by the Imaging Committee. In the case of multiple sites having the same scanners, an import file will be generated by one of the sites (Exam Card – Philips or EXAR file – Siemens) and distributed. This will allow for all systems to have a uniform protocol loaded onto their system without the manual entering of parameters. For other sites, the protocol parameters will be available in PDF format on the MarkVCID website.

2.4 Instructions for Certification Scan

For site certification, a phantom must be scanned using the MarkVCID Human Scan protocol. Since this is a phantom scan, it can be done prior to IRB approval.

- MRI certification will consist of a phantom scan using the human protocol, though the site may be requested to scan a volunteer during the certification process.
- No changes should be made to the protocol without prior approval.
- Sites are encouraged to use the site’s standard head coil used for participant scans and should use the same coil for the site certification scans as well.
- The larger ADNI Phantom may not fit in 64- or 32-channel head coils. Sites are instructed to use any spherical MRI phantom that best fits the coil that will be used for participant scans. The newer ADNI phantom is smaller and generally will fit into a 64- and 32-channel head coils.
- The phantom is not considered to be a study participant and so does not need to be registered as one on the web portal. The certification scan session also does not need to be registered.

2.5 Instructions for Volunteer Certification Scan (*only if requested*)

The CC Imaging Team may request a human volunteer scan with the MARKVCID protocol to complete MRI certification. In this case, your site will be asked to scan the entire protocol on consented human volunteer(s) without modification.

2.6 Naming Convention for Certification Scans

When entering information into the scanner console please use the following naming convention for the participant's name:

Phantom: XXX_P

Volunteer: XXX_V

XXX = 3-digit site number; "P" for phantom or "V" for volunteer

2.7 Data Transfer of Certification Scans

Please archive locally all data acquired for site certification according to your site's standard practice and upload the scan via Globus (Please refer to the Data De-Identification and Globus Data Transfer section later in this manual.)

2.8 Site Certification Scan Results

The MarkVCID Coordinating Center Imaging Quality Control (QC) team will perform a QC evaluation on the phantom and/or volunteer scan data within seven business days of receipt. The QC team will review for correct parameters, good image quality and scanner performance to ensure that there are no other underlying problems have occurred during scan sessions. After successful certification an official Site Certification letter will be sent to the site contacts notifying them their site has been approved and may now scan participants. If the scans do not pass the QC evaluation, the site may be asked to re-scan after making the suggested changes by the CC Imaging team.

3. Hardware and Software Upgrades

To avoid any delays or issues in scanning, the MarkVCID Imaging Team requires notification **at least 4 weeks** prior to any software and/or hardware upgrades for an already-certified scanner in the MarkVCID study. This is to ensure that there is sufficient time to identify necessary changes, and the upgraded scanner can be re-certified.

At the time of the MRI scanner upgrade, you will be required to again scan a phantom prior of the entire MarkVCID protocol before scanning of further study participants and submit the data for QC evaluation.

If a site fails to perform the phantom scans and receive certification prior to a participant being scanned on the upgraded scanner, MarkVCID may not accept the participant scans. Sites must allow 7 business days for QC of the phantom scan, and as such, participant scanning should be scheduled accordingly. The study coordinator and the principal investigator at the site will be notified if a phantom scan has not been received and approved within the appropriate time frame.

If you have questions regarding this procedure, please contact the MarkVCID Imaging Team using the email address and subject line given in the Contact Information table at the top of this document.

4. MRI Participant Pre-Scan Procedures

4.1 Participant Pre-screening

All participants should have been screened by the consenting study coordinator for standard MRI contraindications at enrollment. Participants must also be screened for MRI contraindications immediately before the MRI scan using your local MRI contraindications form. Contraindications include, but are not limited to:

- Non-removable ferrous metal objects
- Shrapnel
- Metal fragment in the eye
- “Triggerfish” contact lenses
- Aneurysm clips
- Pacemakers
- Ear implants
- Gastric reflux device
- Spinal nerve stimulators
- Permanent makeup
- Defibrillator

4.2 Participant Safety and Monitoring

- The site should follow their standard participant consent protocols as approved by the appropriate IRB(s).
- Site staff should first explain the scan procedure to the participant, so the participant knows what to expect during the MRI.
- The participant should be given the opportunity to use the restroom before the scan begins.
- Follow local MRI safety procedures and refer to the above pre-screening list.
- Provide each participant with hearing protection.
- Use local standard practice for monitoring the participant during the scan. Check in with the participant often.
- Have the participant remove all upper body clothing with metallic components, such as zippers, buttons, underwire bras, that may cause artifacts in the MRI images. Your site may require the participant wear a specific gown.
- Ensure that standard MRI bay entry exclusions are followed, and ensure that the participant has removed their dentures as well as any hair clips, combs, earrings, necklaces, etc.

4.3 Head Coil Selection

MarkVCID sites are encouraged to use the head coil giving the highest quality images. Typically, this is a 64- or 32-channel head coil for most Siemens and Philips scanners. This is particularly important for multiband scans.

4.4 Participant Positioning

1. Proper participant positioning is extremely important in obtaining high-quality data. Studies have shown that correct, consistent head placement can significantly reduce the degree of image distortion. Therefore, it is important that each participant is positioned in the same manner for each and every MRI exam.
2. Please follow the procedures below for positioning the participant:

- Place clean sheet on scanner table and coil cradle.
- Provide each participant with ear protection.
- Position the participant so their head and neck are relaxed, but without rotation. Proper placement in the head coil is crucial because some scans will be 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 rejection and trigger a request for a re-scan.
- 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 the participant has been positioned, place foam supports along the sides of head for stabilizing support and reduction of motion. If a forehead strap is available at your site, please use it.
- Align the centering crosshairs on the participant's nasion (directly between the patient's eyebrows) at every scanning session.
- Center the patient's head in the head coil, making sure the participant is elevated enough in the coil to prevent signal loss at the inferior portion of the brain.
- Each participant should be given a panic button or squeeze ball for emergencies or the onset of claustrophobia.
- Staff should remind the participant to hold as still as possible during the scan.

If a deviation from these instructions is required to accommodate a participant, the MRI technologist should notify the MarkVCID QC team by including a description in the Comments section on the Scan Session Registration webform on the MarkVCID website while registering the scan session data.

5. MRI Protocol

Each participant scan should use the harmonized MarkVCID protocol relevant for the vendor and software version of your site's scanner. During QC, all scans will be checked to ensure that the correct protocol was used. All scans should be performed on the scanner that was used in the site imaging certification process. The scanner used for each scan will also be checked during the QC process and scans on non-certified scanners will be rejected and a rescan requested.

If your site is using multiple MRI scanners, **please ensure that each participant is scanned on the same scanner using a head coil with the same number of channels at all timepoints, whenever possible**. The only exception to this directive is when the original scanner is no longer available for scanning. Even when a scanner has hardware or software upgrades, it is still preferable to use the same scanner. The performance of longitudinal scans using the same hardware reduces variability and increases data quality. To track scanner information, we have provided the Registered Imaging Log Template available on the MarkVCID website under MarkVCID2 Protocols and Resources → Imaging Management Resources. When scheduling follow-up scans, please consult the Log to determine the correct scanner. Any questions should be directed to the MarkVCID CC Imaging Team.

5.1 Human Scan Protocol and Scan Order

1. 3-Plane Localizer
2. Sagittal 3D T1 Weighted Sequence (ME-MPRAGE)
3. Sagittal 3D FLAIR
4. Axial DWI PA (Multi-band if possible, b=1000, 6 b=0, 40 b≠0)
5. Axial DWI AP (Multi-band if possible, b=1000, 2 b=0, 6 b≠0)
6. Sagittal 3D T2 SPACE
7. Sagittal 3D ME T2 GRE
8. 3-Plane Localizer
9. Axial BOLD for CVR

The above order should be used for the scans. Successful completion of the first 5 scans in the above protocol will be considered a "complete" scan, but every effort should be made to acquire the full protocol on each participant. The second localizer is required since the patient must be removed from the bore to supply the breathing apparatus for the CVR scan.

The MarkVCID QC team will review all imaging data within seven business days of receipt. If the MarkVCID protocol sequences were not used or incorrect acquisition parameters, the scan may be rejected and a rescan requested. Scan quality will also be monitored and a rescan may be requested if there is excessive motion or poor image quality. For this reason, an initial data-quality check should be made at the scanner and scans repeated during that same scan session if the quality is poor or there is excessive participant motion.

If a repeated scan is not possible or the data is determined later to be unusable, you may be asked to rescan the participant. The chart below shows which sequences need to be completed (indicated by an "X") when a rescan is requested. For example, if the Sagittal 3D FLAIR scan is unusable and a rescan is requested, you should also acquire a Sagittal 3D T1 weighted scan during the rescan session. Note that a Sagittal 3D T1 weighted scan is required for all rescan sessions (except Axial BOLD for CVR) as this is needed for the registration step of the data processing. In addition, if either the Axial

DWI PA or Axial DWI AP scans are missing or unusable, and a rescan is requested, please acquire both scans, as well as a Sagittal 3D T1 weighted scan. If multiple scans are unusable, repeat the sequences indicated by an "X" in the chart for both scans. For example, if the FLAIR scan and the CVR scan were both unusable, then the T1-weighted, FLAIR, and CVR sequences would need to be repeated.

During the scanner certification process, the Series Description (name) of each scan was specified and checked. Please do not modify the Series Description of the rescan as it is used in the automated scan-type identification pipeline at data upload. If a scan type acquisition must be repeated, please do not modify the Series Description to indicate that the later scan is a rescan. Repeated sequences will be identified by the acquisition time.

Missing or Unusable Sequence	Sagittal 3D T1 Weighted (ME-MPRAGE)	Sagittal 3D FLAIR	Axial DWI PA	Axial DWI AP	Sagittal 3D T2 SPACE	Sagittal 3D ME T2 GRE	Axial BOLD for CVR
Sagittal 3D T1 Weighted*	X	X	X	X	X	X	X
Sagittal 3D FLAIR*	X	X					
Axial DWI PA*	X		X	X			
Axial DWI AP*	X		X	X			
Sagittal 3D T2 SPACE	X				X		
Sagittal 3D ME T2 GRE*	X					X	
Axial BOLD for CVR							X

*required sequence

5.2 Acquisition of MRI Images

Please use only the approved sequences from the MarkVCID harmonized protocol to collect data in this study. Changes of parameter values will be detected by the QC process and may be cause for rescan request.

When naming each sequence on the scanner, the following naming convention should be used (note that underscores, rather than dashes are also allowed):

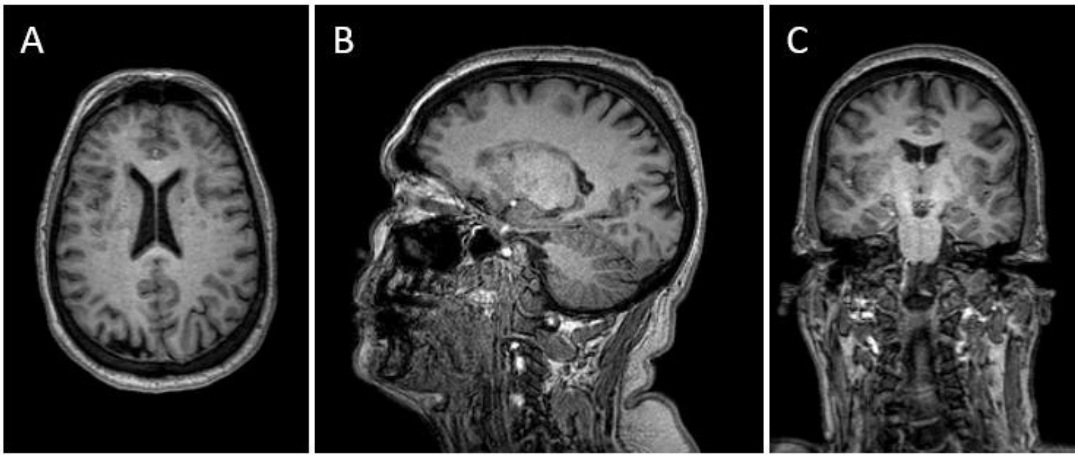
1. Localizer
2. Sag-3D-T1-MEMPRAGE
3. Sag-3D-FLAIR
4. Ax-DWI-PA-40-6
5. Ax-DWI-AP-6-2
6. Sag-3D-T2-SPACE
7. Sag-3D-ME-GRE
8. Localizer2
9. Ax-CVR

The consistent naming of scans allows the Data Management Core (DMC) to simplify the data preparation process (see the Preparation and Transfer section of chapter 7 of this document, Data Handling Overview).

In the following sections, we show examples of correct head placement and of each image type required by the protocol.

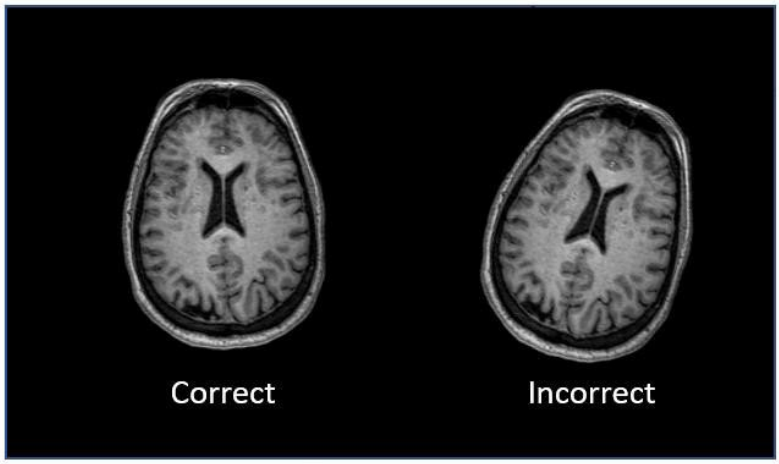
5.3 Three-plane Localizer, Head Orientation, and FOV Box

The localizer should be used to ensure that there are no wrap-around artifacts in the acquired data and that the brain is entirely covered by the bounding field-of-view (FOV) box. This is shown below.



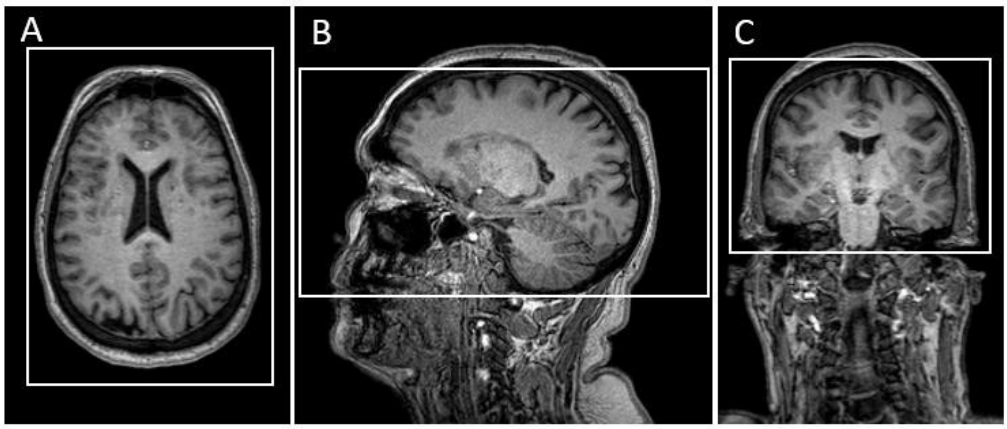
3-Plane Localizer

- **<u>Please make sure that the participant is positioned properly and consistently, as this goes a long way to minimize differences/distortions between scan sessions.</u>** If the participants head is tilted, please adjust the participant's orientation in the head coil and re-run the localizer. Continue this process until the participant is correctly centered in the head coil.



Head Orientation

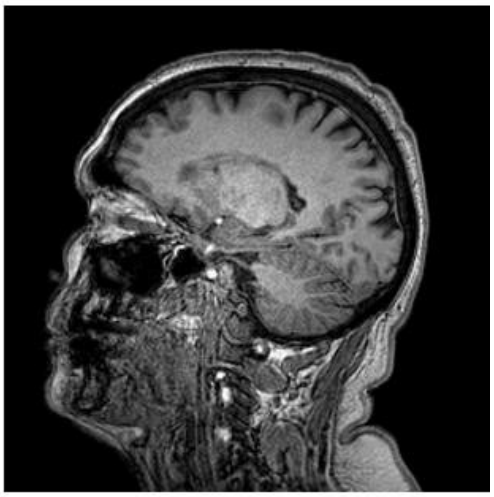
- Once the participant is positioned correctly, begin running the MarkVCID protocol.
- **NOTE: The <u>entire brain</u> must be covered for <u>all scans</u>. See the figure below for examples of the correct "slice box" (the bounding box around the brain that should contain the slices).**



Slice “boxes”

In the axial view (A) center the field-of-view box around the center of the brain to avoid any wrap-around artifacts. In the sagittal view (B), please ensure that the field-of-view box is wide enough to avoid the nose wrapping around the image. In the coronal view (C), center the field-of-view box such that the top and bottom of the brain are fully enclosed.

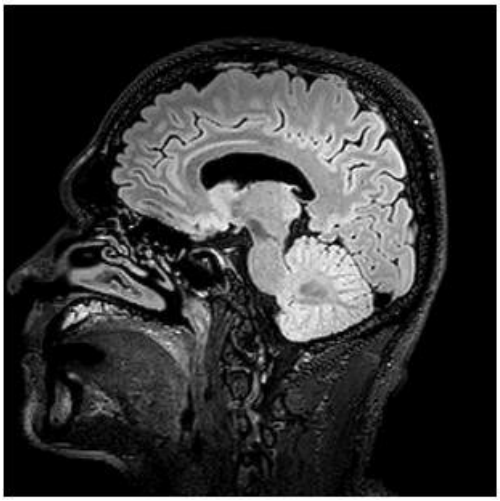
5.4 Sagittal 3D T1 Weighted Sequence (ME-MPRAGE)



Example of an accelerated sagittal 3D T1-weighted scan

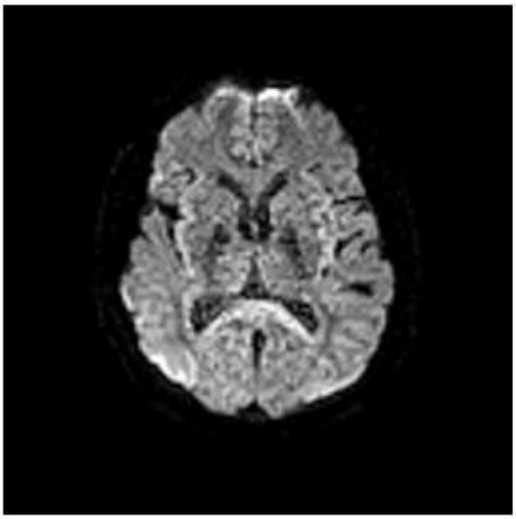
Visual inspection of the T1-weighted scan should be performed at the scanner to ensure that there is good gray/white matter contrast in the image volume and that there is not excessive head motion artifacts.

5.5 Sagittal 3D FLAIR



Example of a sagittal 3D FLAIR

5.6 Axial DWI P→A Scan (Multi-band if possible, b=1000, 6 b=0, 40 b≠0)

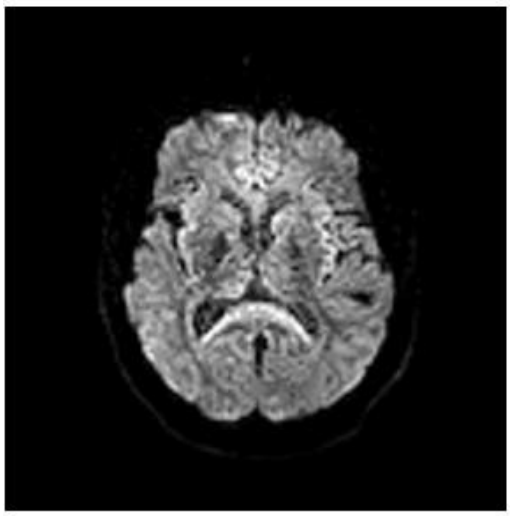


Example of axial diffusion-weighted image (DWI) with phase-encoding direction set to P→A

DWI P→A Scan (Multi-band if possible, b=1000, 5 b=0, 40 b≠0)

Scanning Notes: The phase-encoding direction of this scan is set to P→A. MarkVCID is using a specific set of diffusion gradient directions, not the vendor-specific set found as default selections on your scanner. A file containing these diffusion gradient directions are available on the MarkVCID website in both Siemens and Philips formatting. Again, please use only “straight” axial slices (i.e., non-oblique).

5.7 Axial DWI A→P Scan (Multi-band if possible, b=1000, 2 b=0, 6 b≠0)



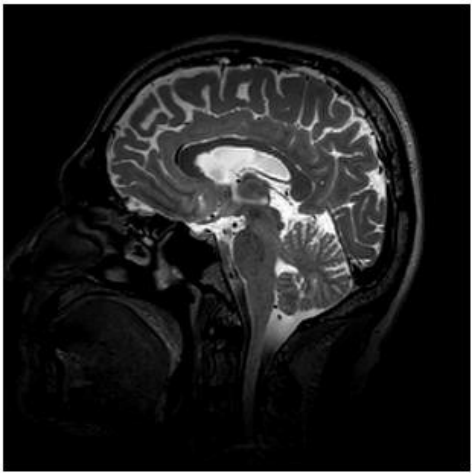
Example of axial multi-band diffusion-weighted image (DWI) with phase-encoding direction set to A→P

Notes: The two DTI sequences are different (the first has longer duration than the second and has a different phase-encoding direction – P→A versus A→P, respectively). These two scans will be used to correct the P→A scan for image distortions due to the use of the EPI acquisition method. Also, please do not deviate from the prescribed number of b=0 and b≠0 scans in the A→P scan as this can cause issues with the writing of the parameter information into the file headers.

Scanning Notes:

- **Please use the Copy Ref to the slices and center of FOV from the previous DWI Sequence**
- **On Siemens Systems <u>only</u>, this will result in the Phase Encoding Direction to set to R>>L**
    - **To correct this, you will need to open the Phase Encoding Option and manually set to A→P**

5.8 Sagittal 3D T2-weighted SPACE

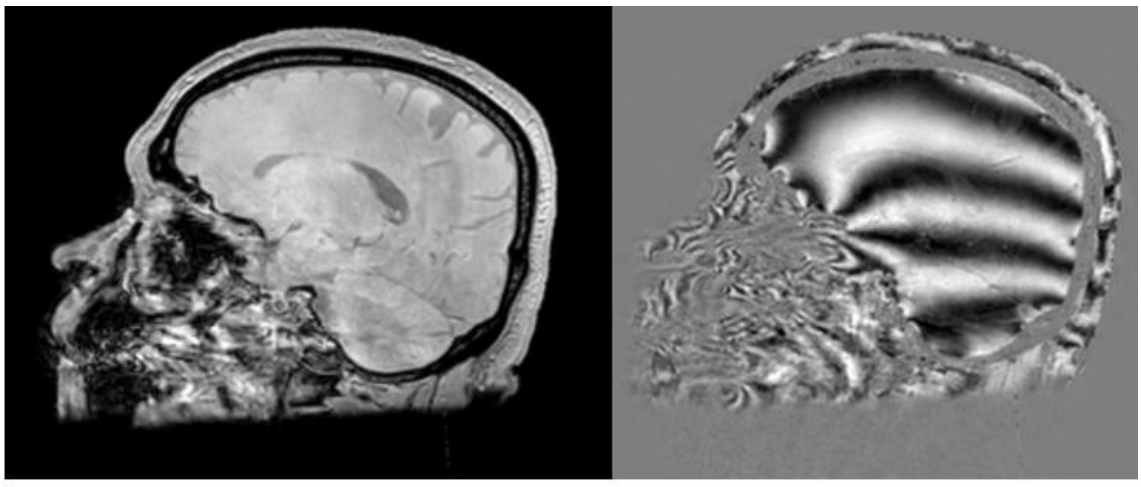


Example of a sagittal 3D T2-weighted SPACE scan

Scanning Note: Please use the Copy Ref to the slices and center of FOV from the Sagittal 3D T1-Weighted Sequence

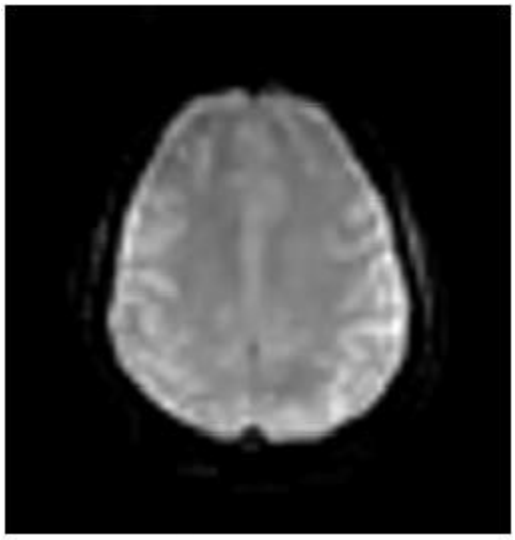
5.9 Sagittal 3D Multi-echo SWI/GRE

This scan collects multi-echo GRE data that will be used to construct a susceptibility-weighted imaging volume. While it is possible to have the scanner calculate and output this volume, exach scanner vendor implements the SWI calculation using a different algorithm. In order for the SWI results for MarkVCID to be comparable across sites then, we ask that you do not select the calculation of the SWIs on your scanner console but instead collect the raw data necessary to do the calculation offline. Your scanner may output either Magnitude/Phase or Real/Imaginary images. These data are to be sent to the MarkVCID RC.



Example of a Sagittal GRE dataset exported as a Magnitude and Phase dataset

5.10 Axial Bold for CVR



Example of an axial BOLD scan for measurement of CVR

- Positioning: Position on mid-sagittal slice from tri-planar localizer.
- Please remember to acquire the CO_2 recording file and include it in the data that is transferred to the DMC.

Scanning Note: Site staff must be trained in advance to perform CVR scanning. Please ensure that site staff have undergone the required training before attempting to acquire CVR data. Please ensure that Phase Encoding is set to P→A prior to scanning for Siemens and that the fat shift direction = "P" for Philips.

6. MRI Participant Scan Procedures

6.1 Entering Participant Information into the Scanner

The MRI Technologist should enter the participant information into the scanner per the local site's standard though, if possible, please enter the Participant ID in the Patient Name field and Patient ID fields. The scan header will be de-identified and rendered HIPAA compliant as part of the data preparation workflow before transferring the data to the DMC via Globus (see Data De-Identification and Globus Data Transfer section).

6.2 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 scan should be stopped,

and it should be noted in the EDC system on the Research MRI Case Report Form. An email should also be sent to the DMC including the Participant ID, scan date, timepoint, and the reason the participant was unable to complete the MRI. If the Imaging Technologist conducting the scan does not have access to the EDC, they should notify the lead study CRC and ask them to complete these steps.

If the first four scan sequences - T1-Weighted, FLAIR, and PA/AP Diffusion - or more are obtained, sites should register and transfer these images, making note of the discontinuation in the comment section of the Scan Session Registration Form. See the Registering an Imaging Scan Session and Data De-Identification and Globus Data Transfer sections for details. If those three sequences are not executed to completion, the scan session is not considered to have generated a usable dataset and the scan session should be rescheduled if possible. Please contact the DMC if this occurs.

6.3 On-Site Clinical Reads

Every participant must receive a clinical read by an on-site radiologist or M.D. at the MRI facility. Review of research MRIs for clinically relevant findings and management of such findings should follow standard local practice at CPSs. Scan interpretations for diagnostic clinical purposes will **not** be provided by the MarkVCID DMC or as part of the centralized imaging analysis. If there are findings on a particular set of scans, please consult the MarkVCID imaging biomarker set of exclusion requirements, which will be determined by the Imaging Subcommittee and posted on the website. If the participant does not meet any of the exclusion criteria, the data can be sent to the DMC and the patient continued in the study. If the findings do meet one or more of the exclusion criteria, please contact the DMC to determine the course of action which will depend upon the participant's current timepoint.

6.4 Archive Procedures

Every MRI scan for the MarkVCID study must be archived onsite following your site's standard practice. Additional data transfers or copies may be requested by the MarkVCID DMC in the event a data transfer is interrupted or incomplete. Possible MRI archive mediums include PACS or other non-volatile media storage.

6.5 Request for Repeat/Additional MRI Scans

A re-scan may be required in the event that the T1-weighted, FLAIR, diffusion-weighted, and/or gradient-recalled echo scan(s) are found to be unacceptable due to participant motion or an incomplete/incorrect MRI acquisition.

The MarkVCID QC team will check all MRI scans to be sure that the exam was conducted on the site's scanner certified for the MarkVCID study, and that the correct electronically loaded sequences have been used to scan each participant. Repeat exams may also be requested if the incorrect scan sequence, orientation, or angulations were used. It is imperative to use the MarkVCID approved protocol sequences with each MarkVCID participant.

6.6 Scan Submission

De-identified data must be transferred to the MarkVCID DMC by uploading scans via the Globus data transfer service (see the Data Handling Overview and the Data De-Identification and Globus Data Transfer section).

6.7 Participant Anonymization Nomenclature

The site will be responsible for anonymizing all patient specific information according to local laws and regulations. In addition, the following DICOM fields must be present. DICOM tags that must be overwritten by the requisite ID's are also noted.

DICOM Tag	Attribute Name	Comment
(0008,0020)	Study Date	
(0008,0021)	Series Date	
(0008, 0060)	Modality	
(0008,0070)	Manufacturer	
(0008, 1030)	Study Description	
(0008,103E)	Series Description	
(0010,0010)	Patient Name	Overwritten With Participant ID
(0010,0020)	Patient ID	Overwritten With Participant ID
(0018,0080)	TR	
(0018,0081)	TE	
(0018,1000)	Device Serial Number	
(0018,1020)	Software Version	
(0018,1030)	Protocol	
(0020,000D)	Study Instance UID	
(0020,000E)	Series Instance UID	
(0008,0080)	Institution Name	Overwritten with the Site ID

Participant ID FORMAT:10 character randomly generated string Participant ID

For example, the Patient Name tag would be coded: E42C5F97B3

6.8 Data Transfer Method

The MarkVCID study will use the Globus data transfer service to transfer data between the MarkVCID Study Sites and the MarkVCID DMC where the data will be stored. Separate transfer to the MarkVCID QC team is not necessary.

See the Data De-Identification and Globus Data Transfer section for details on setting up a Globus account, installing the Globus software, and transferring the data. Sites should transfer the data via Globus within 3 weeks of acquisition.

7. Data Handling Overview

To handle MARKVCID imaging data, each site staff member who will be preparing and transferring data must be certified. The certification process is 1) watch a set of videos on SkyPrep that cover the process and read the Imaging manual sections that pertain to the preparation and transfer of data and 2) register, de-identify, prepare, and transfer a SINGLE dataset. This dataset will be evaluated by DMC staff and certification will be given after successful completion of those steps.

Introduction to the Management System: The MarkVCID data management infrastructure uses a "register/record" system, meaning that you, as the site, register the scan session so the DMC knows how to interpret it, and the DMC records those data into the MarkVCID system. The workflow for both baseline datasets and those from later timepoints is the same: the datasets are 1) registered, 2) de-identified, and 3) transferred to the DMC in that order. Any questions regarding these steps should be directed to the DMC.

Registration: The registration step is performed using the "Scan Session Registration" page that can be found under the "Data Portals" menu visible on the MarkVCID website home page after login. This is a short form that should take less than a few minutes to complete. After submitting the required information at the end of the registration process, you will receive an ID (both on the screen and by email) that will be used to identify the data when you transfer it to the DMC. We recommend storing the Scan Session ID with the participant ID and the date of the scan in a spreadsheet. A template can be found on the MarkVCID website under "Resources" ➔ "Imaging Resources" and the file "MarkVCID Scan Session Log Template".

De-identification: MarkVCID has a specific de-identification standard that is required for data to be accepted. Because of this, it is possible that you will need to perform an additional de-identification step using a software application (your PACS workflow may partially de-identify the data, if that is used to export the data). The DMC recommends DICOM Browser and its use is discussed below (see Data De-Identification and Globus Data Transfer section). If your Radiology Department can perform a custom de-identification, note that the list of fields to be de-identified is contained in the .das file used by the DICOM Browser application and thus that file can be used as a reference. This file is available on the MarkVCID website under the "Consortium Protocols & Resources" page and called "Anonymization Script". To understand the file, however, it will be useful to read the de-identification section of this manual. In addition, the table in section 6.7 of this manual lists the DICOM tags that must be present in the uploaded data in order for the data to be recognized by the data management system. Contact the DMC if additional assistance is required or with any questions.

Preparation and Transfer: Data will be transferred to the DMC using the Globus data transfer service. The anonymized data should be put into a single folder and converted to a Zip archive file before transfer. Instructions for the installation and use of Globus are also presented in this manual (see Data De-Identification and Globus Data Transfer section). Please be aware that Globus is an application that is separate from the MarkVCID website and must be installed on a local computer. We recommend a computer for which you have administrator access, that has access to the internet, and that has access to the data either through a local area connection or through a CD/DVD drive.

Staff Data Handling Certification: To handle MarkVCID imaging data, a site staff member must be certified. The certification process is 1) Read the Imaging manual sections that pertain to the preparation and transfer of data and watch a set of videos on SkyPrep that cover these processes and, 2) attest on SkyPrep to the completion of step 1) and notify the DMC that step 1) is complete, and 3) register, de-identify, prepare, and transfer to the DMC a SINGLE dataset. This dataset will be evaluated by DMC staff and certification will be given after successful completion of those steps.

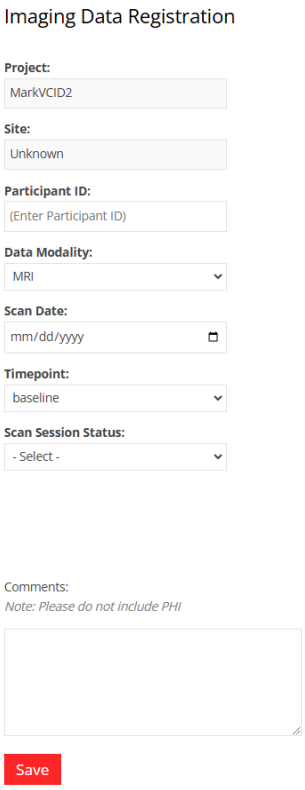
If a site will be using institutional staff to perform the de-identification, organization, and transfer of the data, a MarkVCID site staff member must go through the training steps and act as the contact/responsible staff member for that site. This staff member agrees to act as the liaison between the DMC and the institutional staff performing the data management workflow to resolve issues as they arise.

8. Registering an Imaging Scan Session

8.1 Completing the Imaging Scan Session Registration Form

Each participant MRI scan session should be registered on the MarkVCID website using the Imaging Data Registration page. The goal of this registration is to provide the data management system with some basic information about the scan session and provide the user with a Scan Session ID that will be used when sending the data to the DMC using Globus. Therefore, the scan session should be registered soon after the completion of the session, but before transferring the data to the RC.

To register a scan session, login to the MarkVCID website and select the “Imaging Data Registration” menu item from under the “Resources” menu. You will see the screen below.



The Project item is prefilled as “MarkVCID”. Enter the MarkVCID Participant ID, the image modality, the date of the scan, the time point, and the scan session status. If the scan session was partially completed, specify the missing scan type(s) and select the appropriate reason for the incomplete scan(s). Additional details can be included in the comments section.

Click the “Save” button. All fields must be completed to successfully register a scan session. If the registration was successful, a Scan Session ID number will be displayed on the screen and emailed to you. This ID should be recorded in the MarkVCID Scan Session ID Log Template Excel file that is available through the MarkVCID website under the “Consortium Protocols & Resources” → “Imaging Resources” tabs and clicking the link “MarkVCID Imaging Scan Session Log” template”. The template allows site staff to record the information in the Registration Form for each scan session in an easy-to-use format.

9. Data De-Identification and Globus Data Transfer

9.1 Contact Information

Questions or concerns regarding MarkVCID data de-identification or transfer-related matters should be sent to the DMC.

9.2 Background

This manual contains technical information on the de-identification, organization, and transfer of data to the DMC. It is the responsibility of the site staff involved in these operations to review this document and follow the procedures.

9.3 MarkVCID Project DICOM De-identification

The procedures in this section should be followed exactly.

9.3.1 Purpose

This section of the Imaging Manual instructs users in the use of DicomBrowser to remove Personal Health Information (PHI) from DICOM-formatted files in preparation for transferring the de-identified files to the DMC data management system using the Globus data transfer service.

9.3.2 Overview

DicomBrowser is an application that allows a user to modify the metadata in multiple DICOM files in a single step. This application has a Graphical User Interface (GUI) that provides a user-friendly experience. To use this application, a user supplies DicomBrowser with a de-identification script (anon_for_MarkVCID2.das) that controls which DICOM tags are de-identified. All PHI except for some dates will be removed and users will add the Site and Participant IDs to the files. After editing the script to add the Site ID and the Participant ID, the de-identification process can be applied to all DICOM files from the entire study. The de-identified files should be saved in a separate folder to indicate that the data has been de-identified, which will prevent unwanted alteration of the original DICOM files.

9.3.3 De-identification Procedure

1. Navigate your web browser to the DicomBrowser web page at <https://download.xnat.org/dicombrowser/> and click the appropriate download icon to download and install the application. DICOM Browser is available for all the most popular operating systems (Windows, Mac, Linux).

2. Open the file <anon_for_MarkVCID2.das> (this file will be supplied to each site by the RC) in any text editor (Notepad++, VIM, Emacs, Atom, Sublime Text, etc.). This file is used to tell the program which fields to remove and whether there are any DICOM tag values to be replaced.

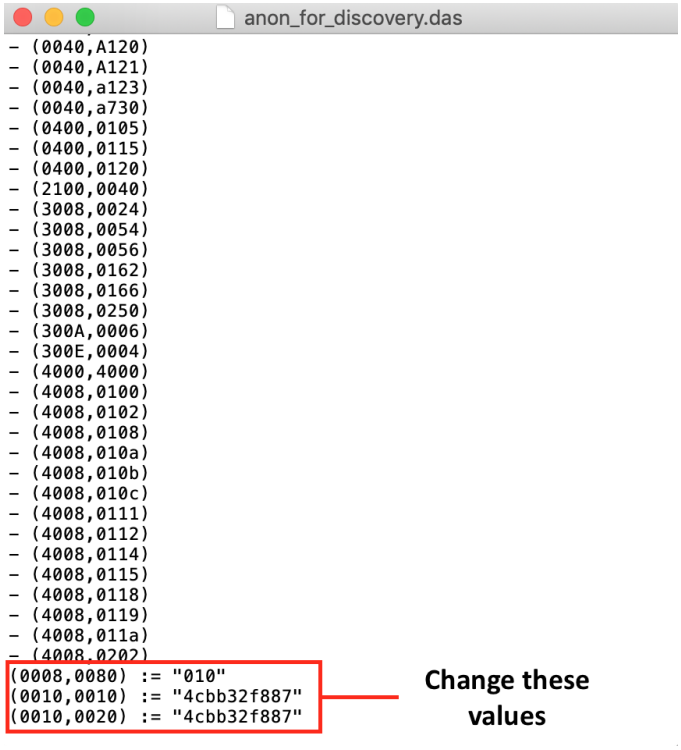
3. Edit the values of the last three lines. Add the MarkVCID Site ID on the line with tag (0008,0080) and add the Participant ID on the lines with tags (0010,0010) and (0010,0020), as shown in the figure below. The Site ID should be entered as a three-digit number, e.g. “010”. Remember that Participant ID’s are assigned when the participant is registered using the Participant Registration web form, so consult your site coordinator if you are unsure of the participant’s ID. Your site coordinator can also supply you with your Site ID. Save your changes to this file.

   Example:

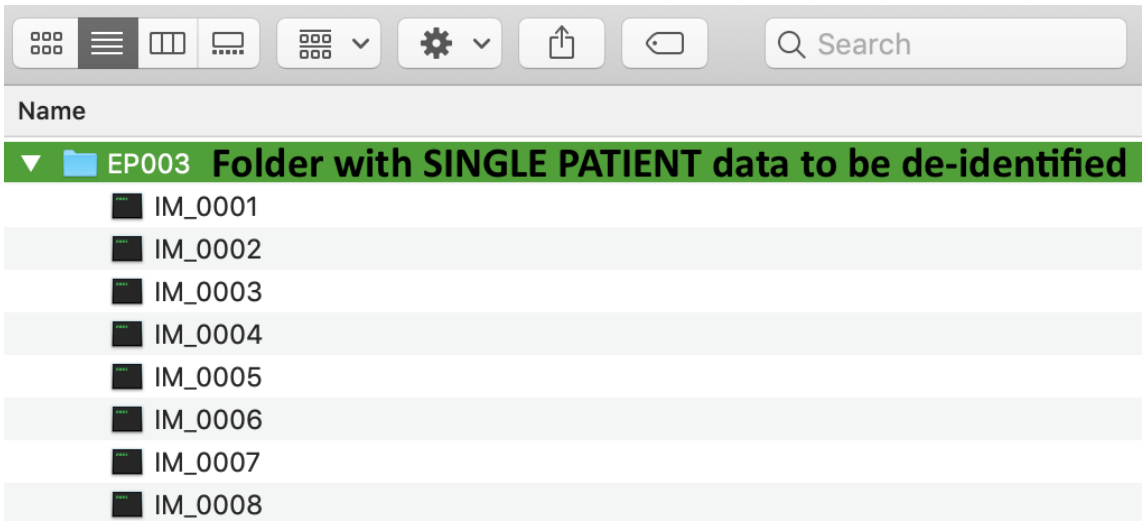
   (0008,0080) := “010”

   (0010,0010) := “4cbb32f887”

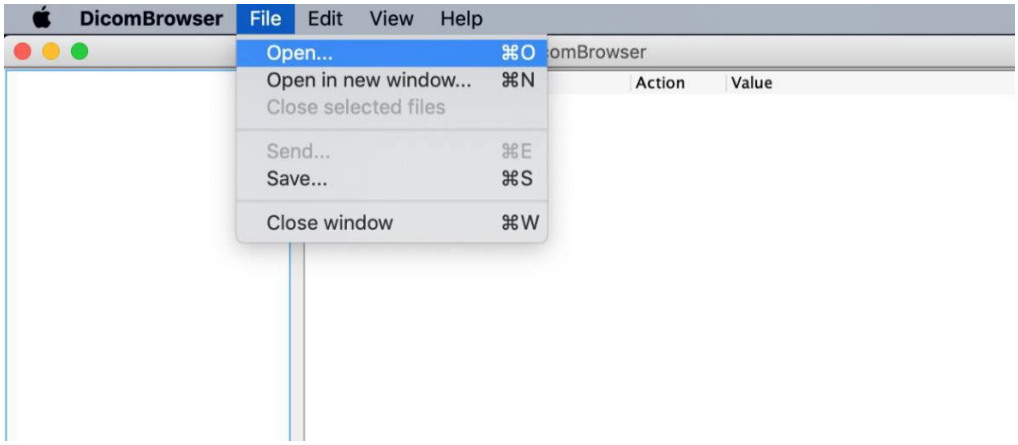
   (0010,0020) := “4cbb32f887”



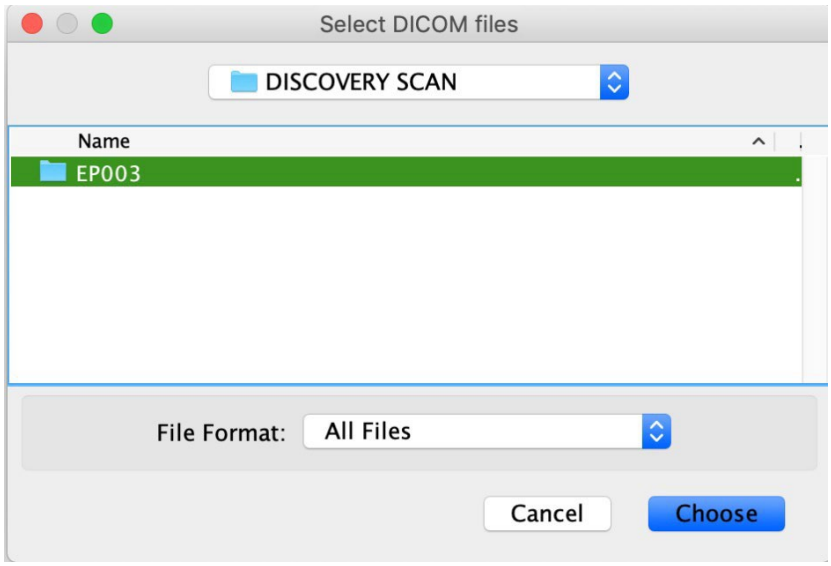
4. All DICOM files for each scan session under a SINGLE Participant should be contained in a single folder. Typically, these files will already be in a single folder after being downloaded from your image storage system or the scanner, but this will depend upon the system at your institution. If the system at your institution places the data in multiple folders, it is not necessary to reorganize the folder structure. The DMC will perform the reorganization. However, please make sure that all the files are de-identified and not only those in a single sub-folder. In the figure below the participant folder is named “EP003”. Please remove any non-image files from the participant folder if any exist.



5. Start the DicomBrowser application and select “File” >> “Open”

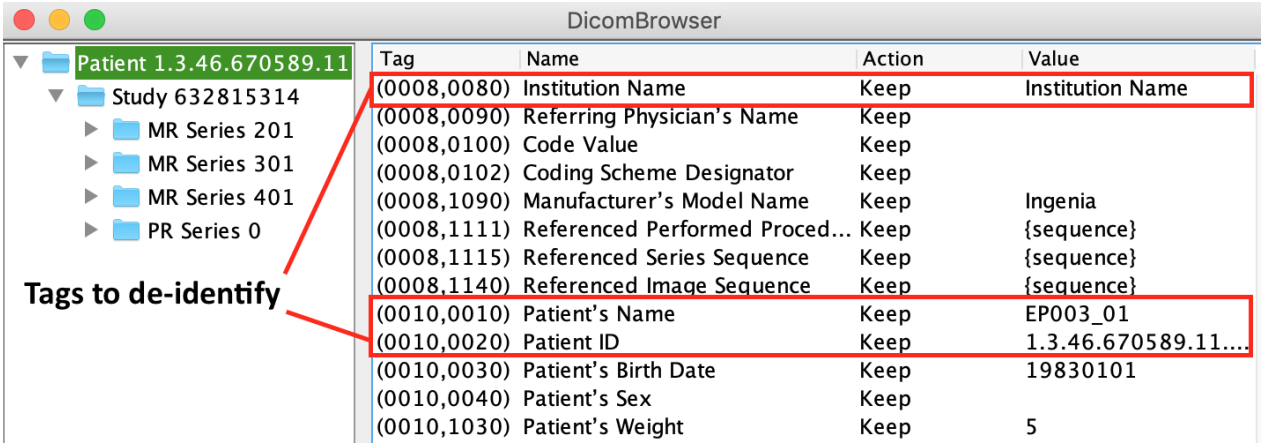


6. Select the folder that holds the original DICOM files for a SINGLE Participant and click “Open” or “Choose” (depending on your computer’s platform).

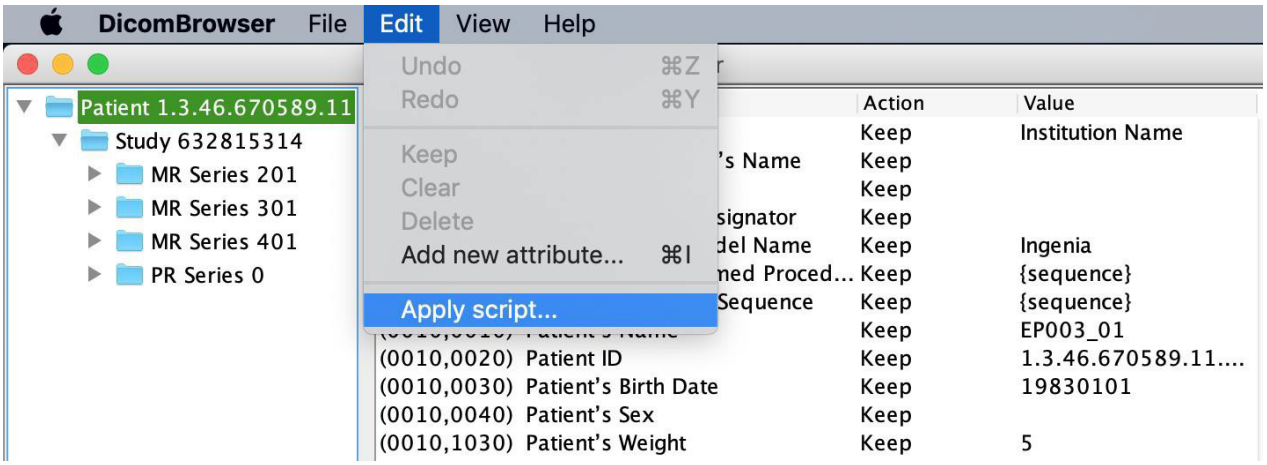


After reading the files, DicomBrowser automatically separates all files by the patient's identifier that was assigned at/by the scanner. This may or may not be the MarkVCID Participant ID. This will appear in the left-hand portion of the user interface. Under each patient identifier folder, DICOM files are further separated by "Study" and then by "Series." If you selected a folder with only a SINGLE Participant, you should only see a single folder tree.

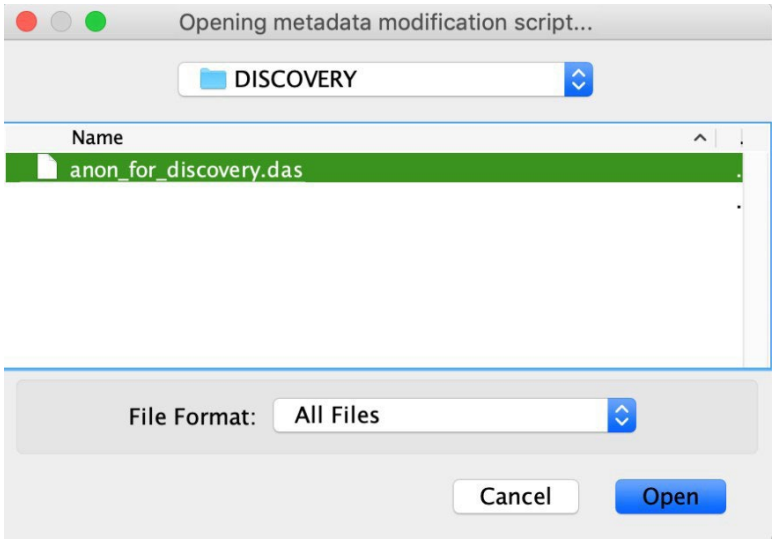
7. To see the image file metadata, click on the participant/patient-level folder on the left and a table should appear on the right with the columns "Tag", "Name", "Action", and "Value." This is the common metadata DICOM tag list for those files. You will be modifying the metadata tags for all the files for that participant.



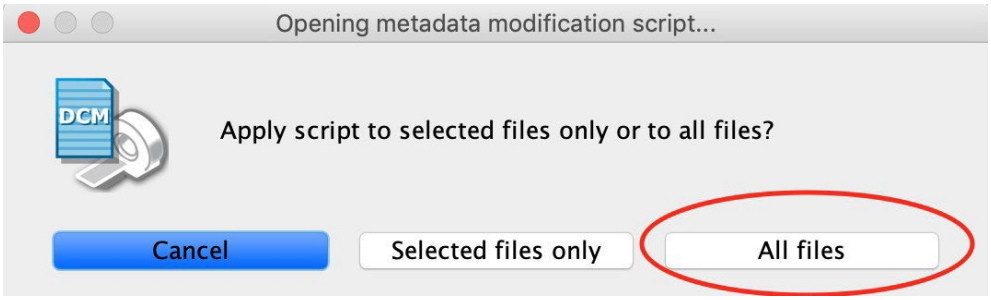
8. To change the Institution Name, Patient's Name, and Patient ID for this patient, click "Edit" >> "Apply script...".



9. You will be asked to select the de-identification script location. Select the <anon_for_MarkVCID2.das> file you modified in step 3 and click "Open".



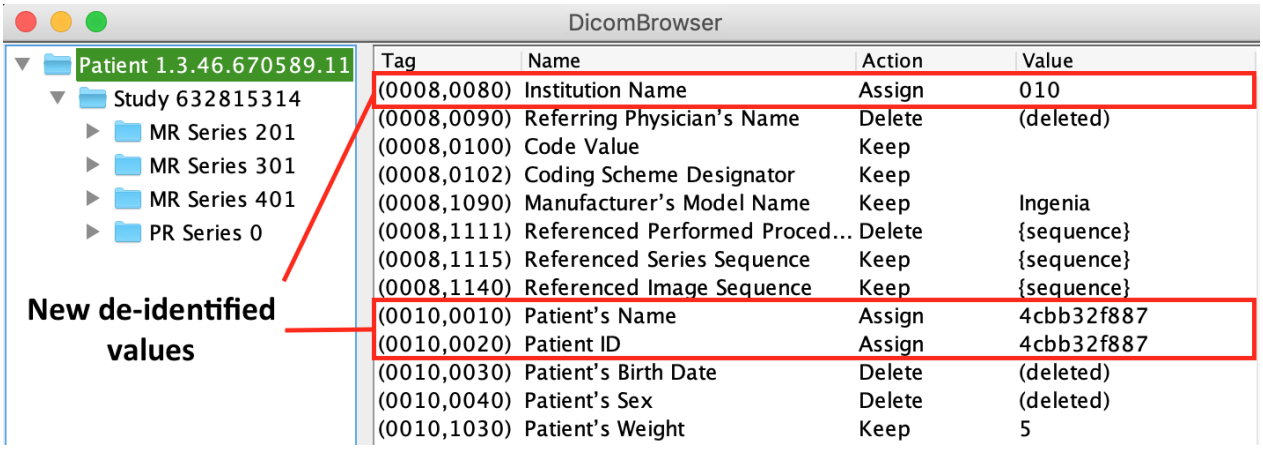
10. Click "All files"



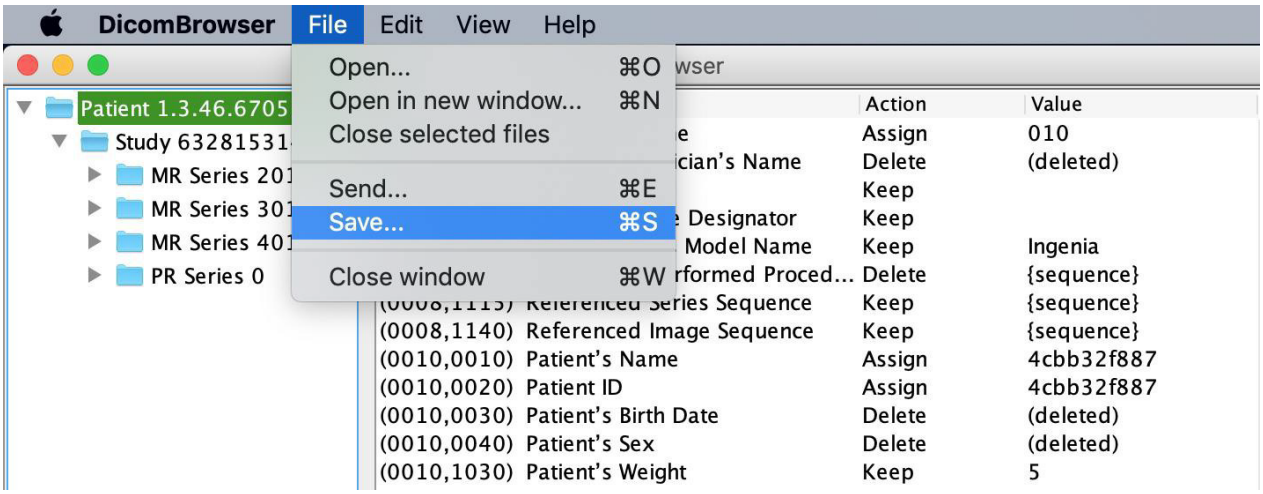
**If DicomBrowser reads multiple patient IDs, as indicated by multiple patient folders in the left-hand pane of the user interface, the folder you selected does not contain data for only a

SINGLE PATIENT. You can select only the patient whose data you want to de-identify by selecting the patient folder and clicking on “Selected files only” after opening the de-identification script. PLEASE ENSURE THAT YOU DON’T REPLACE PARTICIPANT NAME AND ID VALUES ACROSS DATA FROM MULTIPLE PATIENTS!***

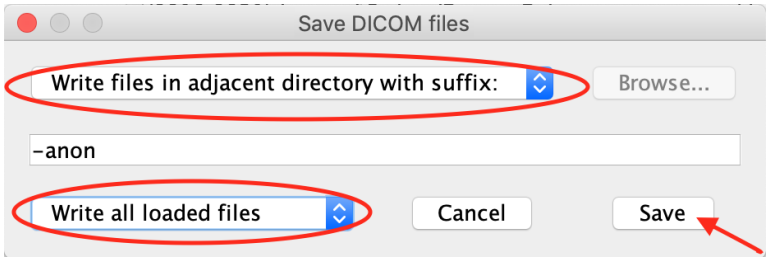
11. Check to see that the script worked. You should see some tags get changed in the “Action” and “Value” columns to “Delete” and “(deleted)”, respectively. The tag whose values were changed will have an “Action” of “Assign”.



12. Click “File” >> “Save”

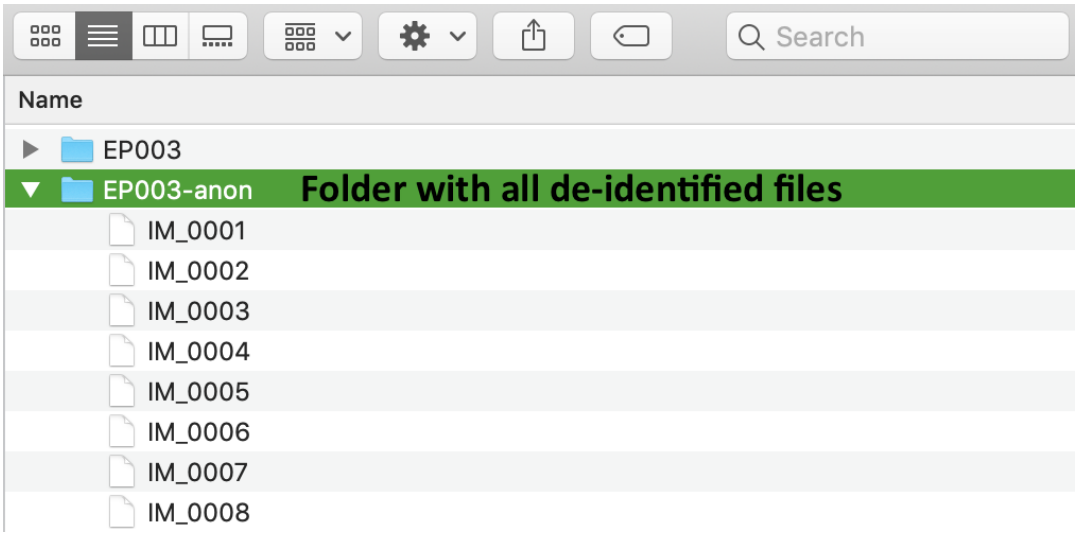


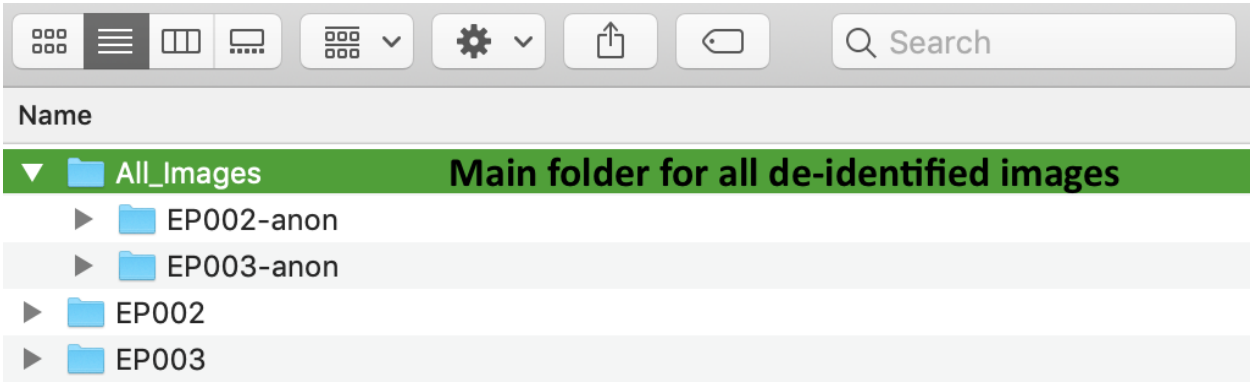
13. Select “Write files in adjacent directory with suffix:” in the top dropdown menu and “Write all loaded files” in the bottom dropdown menu. Click “Save”. In the example below, “-anon” will be added to the new folders name to indicate that these are the modified files.



If you loaded files for multiple patients (see above), you should make sure you only save the de-identified DICOM files for a single patient by first selecting the files, and making sure “Write only selected files” is selected in the bottom dropdown menu

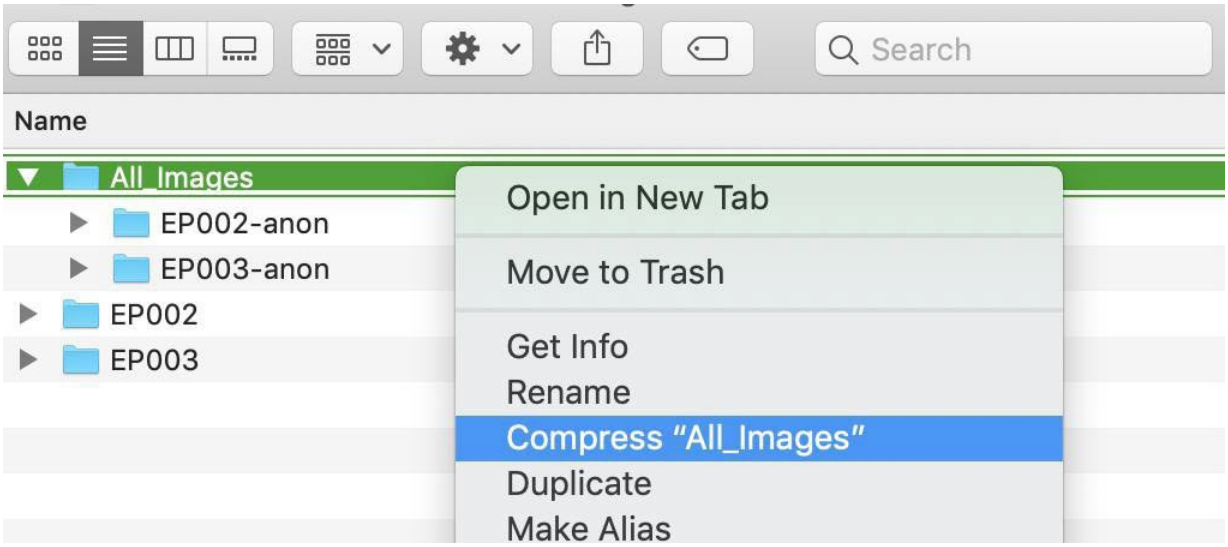
14. This action will create a new folder with the same name, except for the addition of the “-anon” identifier, in the same location as the folder with the original DICOM files. The “-anon” is used to indicate that the output of the de-identification software is written to a separate folder and to ensure that no data is overwritten. Check that the de-identification was performed correctly by opening the “-anon” version of the data into a new DicomBrowser window and checking that the Site ID and Participant ID values are correct.

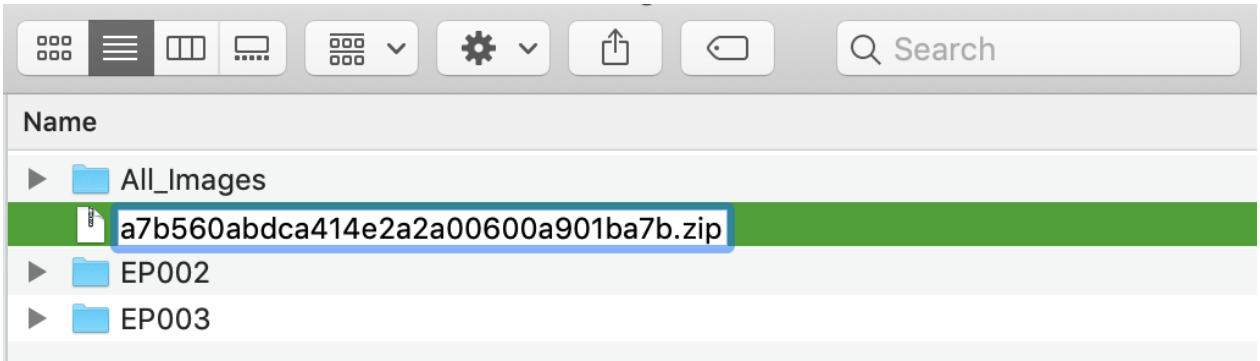




15. **Reminder: If CVR data was acquired, please include the CO_2 recording file in the data folder as well.** Philips CO_2 monitors will generate a .fcd file, while Medtronic CO_2 monitors will generate a .csv file. The CO_2 recording file name should remain unchanged.

    Finally, create a Zip archive of the folder containing the de-identified data and name the archive with the Scan Session ID. To do this on a computer running the **Mac OS**, right click on the main folder and click “Compress”. This will create a zip archive called <folder name>.zip, e.g., “All_Images.zip”. Rename this file to <Scan Session ID>.zip, e.g., “a7b560abdca414e2a2a00600a901ba7b.zip”. This Scan Session ID was emailed to you when you registered the scan session(s) on the MarkVCID website.





If you are using a **Windows** system, right-click on the folder and move your cursor down to the "Send To" option and select "Compressed (zipped) folder". This will create a zip archive called <folder name>.zip, e.g., "All_Images.zip". Rename this file to <Scan Session ID>.zip, e.g. "a7b560abdca414e2a2a00600a901ba7b.zip".

Transfer the zip archive, using Globus, to the MarkVCID shared Globus endpoint (**markvcid#martinosglobus**) into your site's sub-folder in the "/register" folder. Note that you will have to be given access to your site's folder before it will be visible to you on the MarkVCID Globus endpoint. The use of Globus is described in the next section.

9.4 MarkVCID Globus Data Transfer Standard Operating Procedure

9.4.1 Overview

This standard operating procedure describes the steps that will be performed when using Globus to

1. create a Globus online account
2. install the Globus software on a local computer where you have administrator access to, has access to the data for upload, and access to the internet
3. upload MRI data to the MarkVCID Globus shared endpoint (after registering the scan session and de-identifying the data)

9.4.2 Background

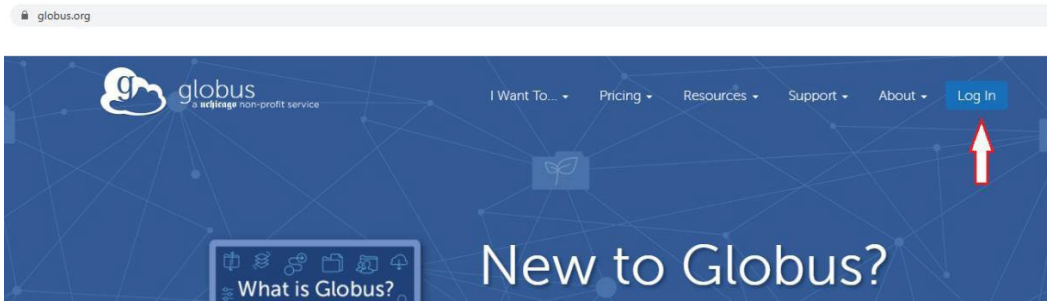
Data will be uploaded using the Globus transfer service (www.globus.org). Globus is built on secure gridFTP and allows for the rapid, robust transfer of large data sets. The use of Globus also allows the user and the DMC to monitor data transfers. Globus consists of two parts: 1) the online interface that allows users to create an account and transfer data from anywhere there is an internet connection and 2) a client (software) on a computer that has access to the data and to the internet. **Both** the Globus account and the client are needed to transfer data, since the online account verifies your identity as a user and the client verifies the source of the data. Note that the Globus client **must** be running on your local computer to transfer data; it is **not** sufficient to only be logged into your Globus online account. It is also important that each person has her/his own account. Please do not create site or group accounts. Individual accounts allow us to

resolve issues more easily and to provide the audit trail for site data transfers required by our security policies.

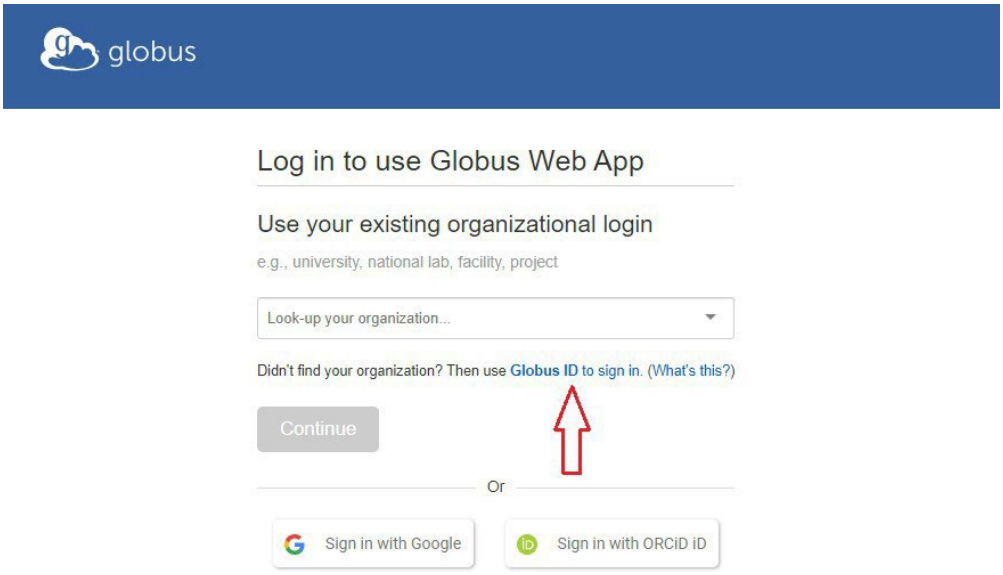
Instructions for creating an account, installing the software, and transferring data are presented in the sections below. The instructions are accompanied by screen shots to help you navigate the process. While the steps are given in detail, the actual process is quick and straightforward. Once the software is set up and running, transfers can be accomplished with only a few mouse clicks.

9.4.3 Creation of a Globus ID

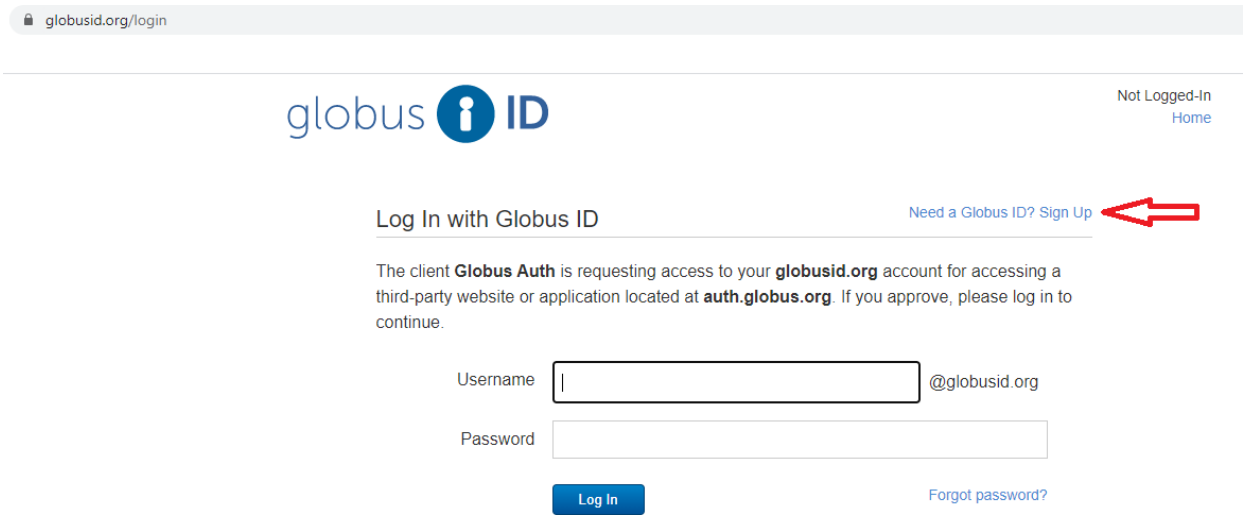
1. Navigate your web browser to https://www.globus.org
2. Click on the blue “Log In” button in the upper right-hand corner.



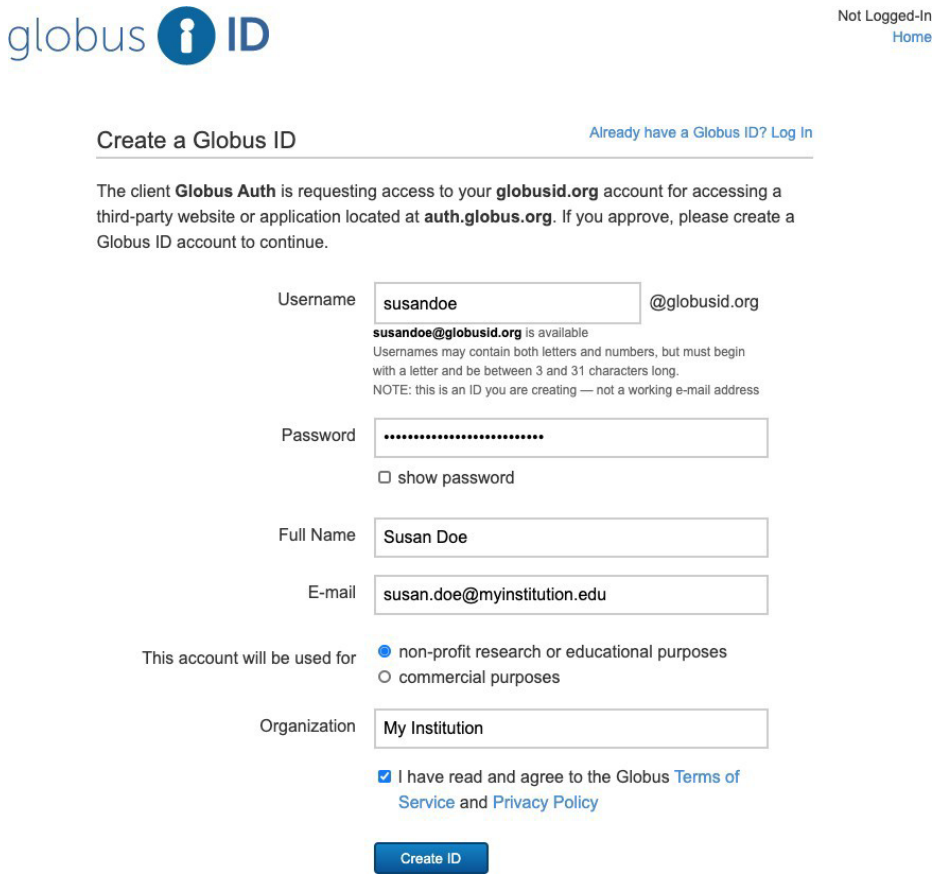
3. Click on "GlobusID to sign in" link (or you can sign in using your institutional login if available under “Look-up your organization”. You can also sign in with your Google account or by using your ORCID ID. To create and use a Globus ID rather than the other options listed above, continue with the following instructions.



4. Click on "Need a Globus ID? Sign Up"



5. Fill out the form using the following model, agree to the Terms of Service, and click "Create ID":



6. Once done, email your personal Globus username along with the name of your site to the DMC so that your account may be granted access to the project folders. If you have signed in using an institutional email, Google email, or other ID, please email this email/ID and your site name to the DMC.

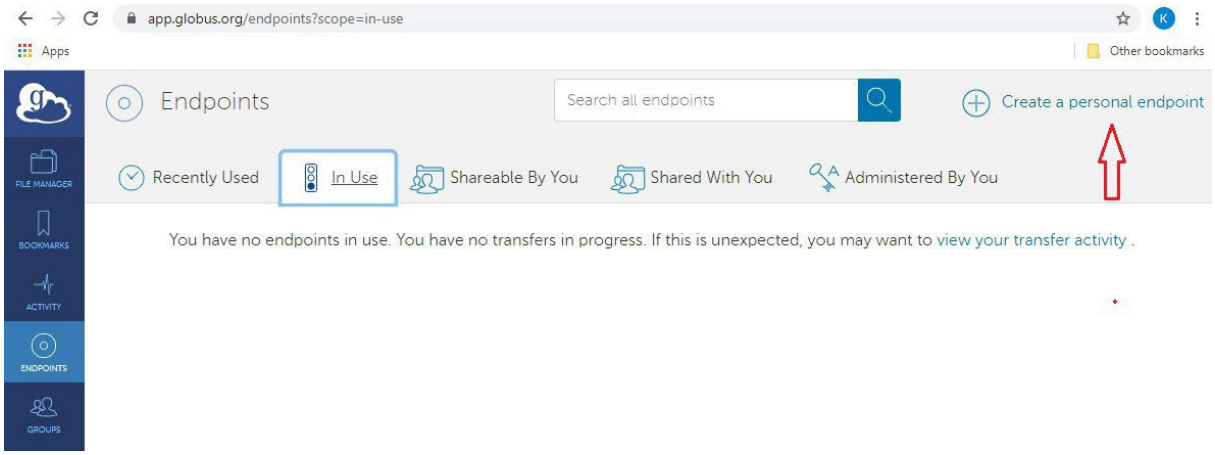
7. Once added to the project, you will receive an invitation email at the email address used in the registration process. Click on the link: “Click here to apply for membership”.

9.4.4 Installing the Globus Connect Personal Client

The installation process creates a personal endpoint on your computer and allows connection to the MarkVCID project’s shared endpoint to which you will be transferring data. Here “endpoint” means that you have a copy of the Globus software on your computer, and it is verified by Globus.

1. Navigate your web browser: to https://www.globus.org and log in.

2. Click on “Endpoints” on the left-hand side of the screen. Then click on “Create a personal endpoint”.

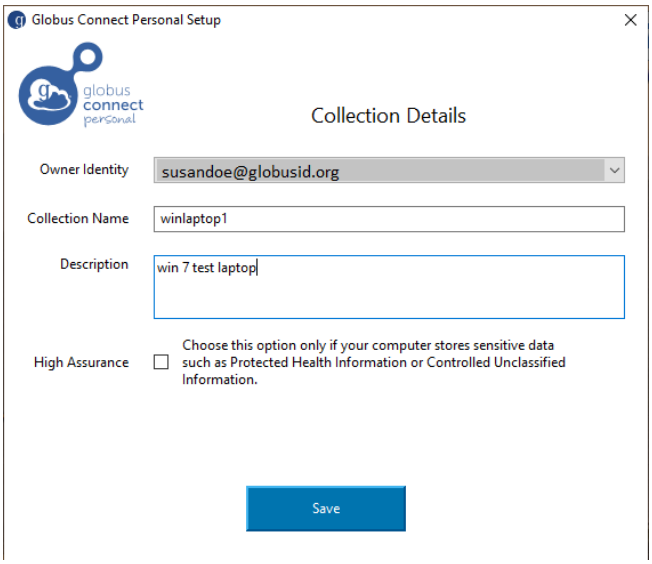


3. Then, click on the download button after verifying that the link is for the correct operating system. You may select a different operating system version by clicking on “Show me other supported operating systems.”

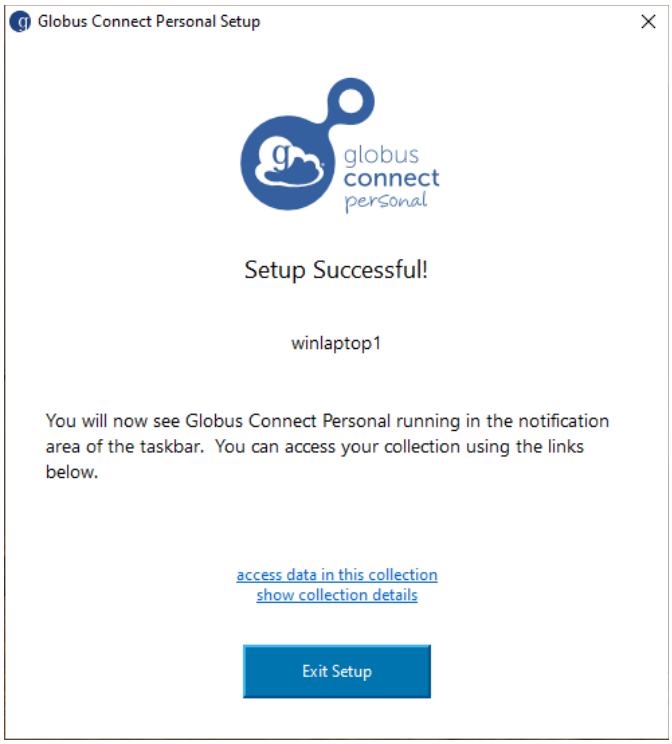
4. Follow the instructions to finish the installation. Select the option to start the Globus client at the end of the installation process.

5. You will then be asked to name your Collection. A Globus Collection is a short name used to identify the computer. We suggest you name your Globus Collection with a mnemonic to help you identify the computer, as you may install the Globus software on multiple computers.

6. Note that only one person can install the Globus software on a computer. Also, note that there is a default folder into which Globus will transfer your files (in Windows this is your Documents folder), but it can be changed. [For instructions on how to further configure your Globus installation, navigate to https://docs.globus.org/how-to/ and click on the link “Install, Configure, and Uninstall Globus Connect Personal for <*your operating system*>.] Click on the “Save” button to finish the Collection setup process.



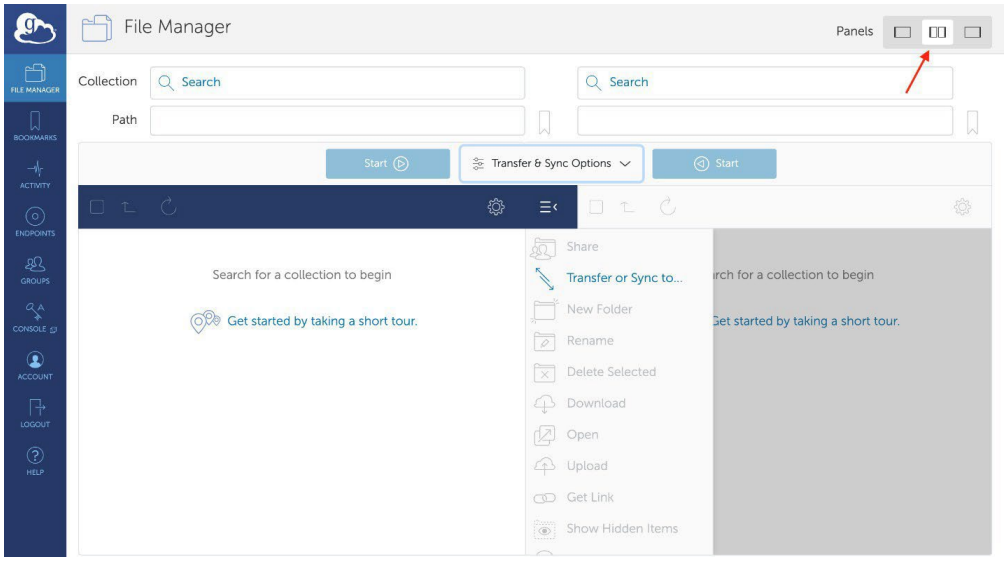
7. If the software has successfully installed, you will see the screen below. Click on “access data in this collection” to view the default folder and begin transferring data. If you have any issues with the installation, please contact the DMC for assistance.



9.4.5 Transferring Files

1. Make sure the Globus application is running on your local computer and log into your Globus account at globus.org

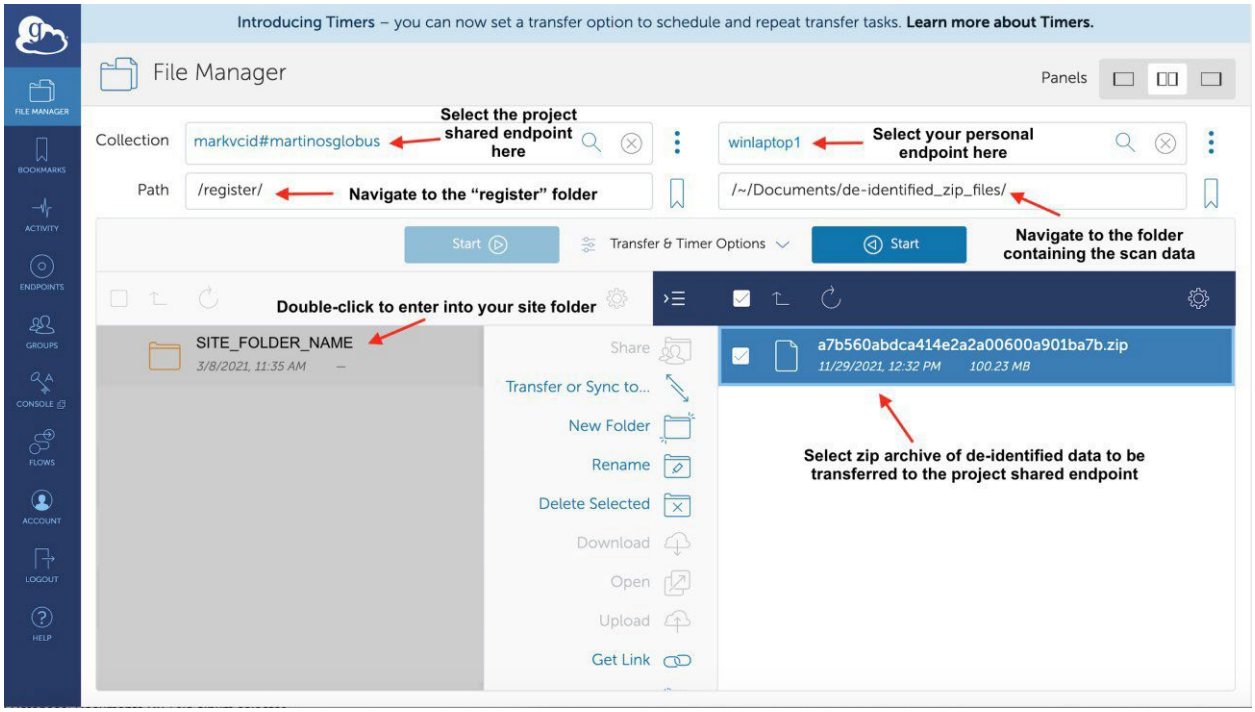
2. Click on the “File Manager” icon from the column of icons on the left-hand side of the window. Be sure to select the two-panel view, which can be selected using the right-hand “panels” icon with two squares on the upper right-hand side of the screen.



3. On the right panel, in the “Collection” box, enter the personal Endpoint name (e.g. winlaptop1) that you setup when you installed the Globus client. Globus will open the folder selected as your default location to begin. Navigate, using either the up-arrow symbol in the dark blue box or the “Path” field, to the directory containing the scan data you wish to send to the DMC.

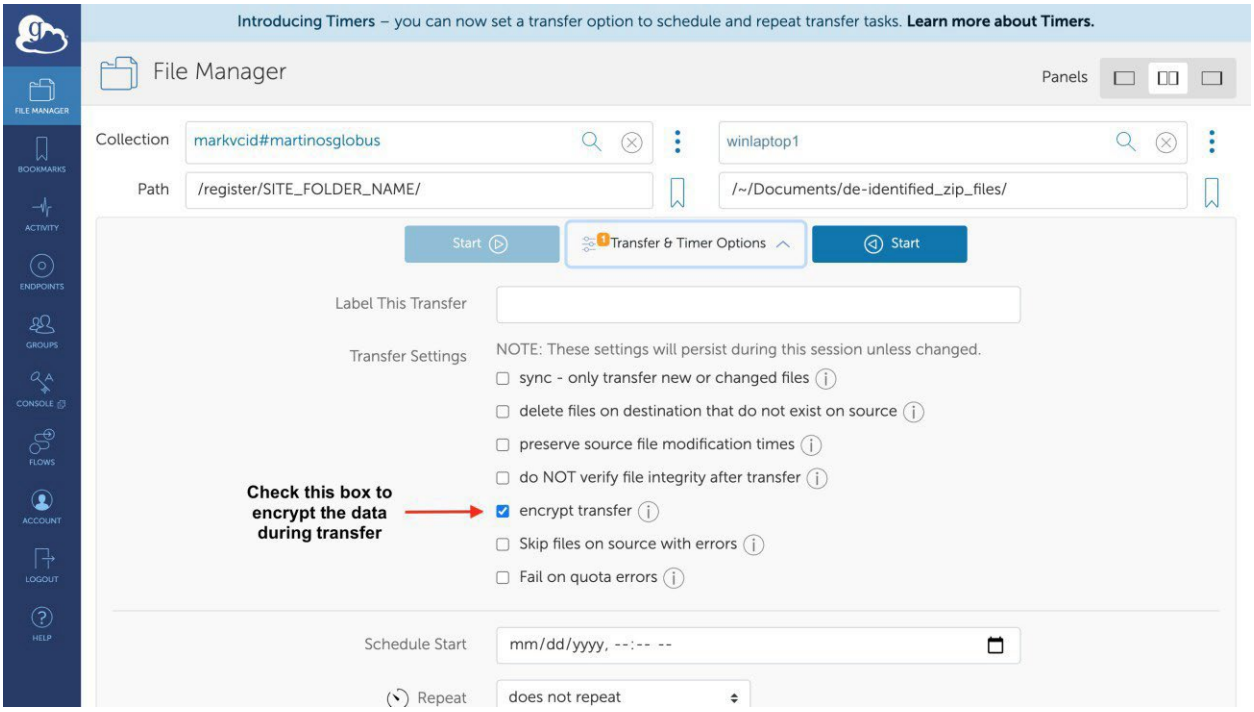
4. **Reminder**: Make sure to put the de-identified DICOM files into one main folder. **If CVR data was acquired, please remember to include the CO_2 recording file in the data folder as well and do not change the recording file name.** Then, create a ZIP archive of that folder named using the Scan Session ID (returned when the MRI session is registered on the MarkVCID portal). The instructions for creating a zip archive are provided above in step 16 of the De-identification section and are also widely available on the web.

5. In the “Collection” pane on the left-hand side of the screen, select the name of the MarkVCID project shared endpoint: **markvcid#martinosglobus** as the endpoint to which the data will be transferred. You will only be able to see this endpoint once you have been given permission so if you are not able to view that Collection, please contact the DMC.



6. Enter into the “register” folder and select the folder named for your site. Again, for that folder to be visible you must have permission to view that folder.

7. Click the dropdown menu for “Transfer & Timer Options,” which will be found in between the two start buttons. Click the checkbox for “**encrypt transfer**” in order to encrypt the data during transfer.



8. Start the transfer by clicking the highlighted blue start button pointing in the direction of **markvcid#martinosglobus**. If the transfer initiation was successful, you will see a message reporting this appear in green. Note that you must keep the Globus program running for the duration of the transfer, but you do not need to keep the Globus web page open. If the transfer is interrupted due to loss of internet connection, the transfer will restart automatically once the Globus software is running again and the internet connection is re-established.

9. You can follow the progress of the transfer by clicking on the “Activity” icon on the left-hand side of the screen in the column of icons. Once the transfer is completed, you will receive an email report with transfer status. If the transfer fails again, please contact the DMC.

Document History

Summary of Changes
MarkVCID2 Imaging Manual

Version	Description of Changes	Reason for Change	Version Date
1.6.1	N/A – original version	N/A	3.17.2022
1.6.2	Revised manual to reflect updated guidance including: • Section 5: Guidance regarding using the same scanner with a head coil that uses the same number of channels throughout the study	Clarification of study procedures	6.24.2022
1.6.3	Revised language to match the imaging protocols: • Section 5.10: Minor update to the language regarding directions	Correction of language to match imaging protocols	7.13.22
1.6.4	Revised manual to reflect updated guidance including: • Section 9.3.3: Added reference to the "Identifying CVR CO_2 Recording Files for Globus Upload" document in step #15	Clarification of study procedures	3.13.2023
1.6.5	Revised manual to reflect updated guidance including: • Section 6.5: Updated the list of scans that may need to be redone if they are unacceptable due to motion or incomplete/incorrect acquisition	Correction of language to match recent updated MOP guidance	4.17.2023
1.6.6	Revised manual with guidance on rescanning participants: • Section 5.1: Added guidance about which sequences would need to be acquired if a rescan is requested	Clarification of study procedures	9.8.2023
1.6.7	Revised manual to reflect updated study procedures including: • Section 8.1: Update to Imaging Data Registration guidance to reflect the updated web form. • Section 9.3.3: Update to step 15 to remove reference to the Nonin CO2 monitor and add the Medtronic CO2 monitor. • Section 9.4.5: Reminder added in step 4 to not change the CVR recording file name.	Update to study procedures	2.27.2025