DOD ADNI

Effects of traumatic brain injury and post traumatic stress disorder on Alzheimer's disease (AD) in Veterans using ADNI

3T MRI Technical Procedures Manual

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I. Contact Information

- If you have any questions regarding the MRI acquisition aspects of this protocol please contact:

adnimri@mayo.edu

- If you have any questions or problems regarding the data transfer to LONI for this protocol please contact:

adni@loni.ucla.edu

- If you have any questions for the ADCS coordinating center protocol please contact:

dod-adni@ucsd.edu

- If you have any questions regarding individual subjects please contact the study coordinator at your referral site.

II. DOD ADNI 3T Study Overview

Study Background

Evidence suggests that both traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD) increase risk for cognitive decline, AD, and dementia. TBI and PTSD are common problems resulting from military service. Thus far, there have been no prospective studies using imaging and biomarkers, which directly measure changes in the brain and AD pathology to study the effects of TBI and PTSD. The DOD ADNI study will provide novel data to test these hypotheses. The results will have major implications for identifying, subjects at increased risk for AD, a possible need for early detection of AD in military Veterans with histories of TBI and PTSD, and a possible need to employ prevention and treatment measures to avoid accelerated development of AD in US military Veterans. This study is a first step toward a larger, more comprehensive study of dementia risk factors in Veterans. The results will lead to a design and statistical powering of a prevention trial. Therefore, this project could be the first step toward the prevention of AD in Veterans, and in the general population.

Using the ADNI infrastructure, this project will use many of the ADNI sites and ADNI methods. But please note the protocol sequence used when conducting MRI scans is unique to DOD ADNI. The protocol sequence installed for ADNI 1 or ADNI GO/2 should NOT be used in this study.

MRI Component

MRI measurements of brain structure have been shown to demonstrate brain atrophy (which correlates with neuron loss) in AD and increasing rates of brain atrophy as subjects become more impaired. Therefore, structural MRI is used as a measure of the rate of disease progression, and possibly as a measure of treatment effect, in AD treatment trials. Structural MRI (MPRAGE/IRSPGR) will be conducted in DOD ADNI and the data will be used both as a measure of the rate of change as well as a predictor of future change, in all study participants. Recently, iron imaging especially micro bleeds (T2 Star/GRE); has been used in anti-amyloid clinical trials, because of the association of microbleeds with anti-amyloid therapy; this will be measured with T2* GRE.

The Core MRI protocol consists of 8 types of sequences that are acquired in every subject, these are: (1) structural Sagittal 3D T1 weighted imaging, (2) IR-SPGR, (3) Calibration, (4) Axial T2 Star/GRE, (5) Axial resting state BOLD fMRI, (6) Axial T2 FSE and (7) Axial Diffusion Tensor Imaging - DTI. (8) Axial T2-FLAIR.

Goals

Primary analyses involve comparing groups on baseline levels of CSF, Neuroimaging (MRI and amyloid PET), and cognitive measures associated with AD pathology and annual change in MRI and cognitive measures to assess whether PTSD or TBI is associated with increased evidence for AD compared to Veteran controls.

Hypotheses will be supported if the TBI and PTSD groups show significantly higher levels of uptake on amyloid PET scans and CSF tau or Ptau than the Veteran controls and significantly lower levels of CSF amyloid beta, MRI volumes, and cognitive function than the Veteran controls.

The specific objectives of the MRI core include: 1) Obtaining high quality multi-site data that is consistent over time. 2) Perform appropriate image quality control throughout the study. 3) Qualify (and re-qualify after upgrades) each scanner on the DOD ADNI MRI protocol. 4) Correct specific classes of image artifacts in each image acquired; imaging intensity nonuniformity, image warping due to gradient nonlinearity, and scaling changes over time. 5) Monitor each scanner longitudinally in the study using the ADNI phantom. 6) Perform quantitative measurements of all images.

Study design for DOD ADNI

All study participants will be scanned using the DOD ADNI 3T scanning protocol. These participants will be scanned during the DOD ADNI clinic visit at Screening and at month 12. Additional follow-up visits may be included, as funding permits.

III. Site Qualification

A. Site Qualification Overview:

Since the DOD ADNI protocol is different from that of the ADNIGO/2 clinical trial, each site will be required to be qualified for DOD ADNI MRI.

Site qualification includes two different exams. The first, being the quality control phantom scans on the specially designed ADNI phantom using the DOD ADNI Phantom QC sequences loaded by your local service engineer. Secondly, your site will be asked to scan a human volunteer with the approved DOD ADNI human sequences loaded by your local service engineer, after your site has received IRB approval for the DOD ADNI protocol. In terms of human scanning, each site will image a volunteer subject with the protocol and send the images to LONI. Each parameter in each of the pulse sequences in the protocol will be checked at Mayo. In the event that the protocol has not been performed according to protocol, the site will be asked to perform another human volunteer scan. This will be repeated as many times as necessary until the site has demonstrated exact execution of the MR protocol in a volunteer subject, at which point they will have passed the human scanning portion of MR site qualification. The volunteers do not need to be elderly controls; in fact scanning for site qualification may be more easily performed with normal younger volunteers. In the event that repeat attempts are needed, repeat scans need not be on the same volunteer subject. Once a site has demonstrated perfect execution of the protocol, the protocol will be stored permanently on the scanner at that site that will be used in the study.

DOD ADNI QC Phantom Scan Protocol:

1) Localizer
2) Calibration Scan
3) QC Phantom IR-SPGR (Accelerated)

DOD ADNI Human Protocol:

(All scans are performed in straight orthogonal planes -- Sagittal or Axial)
(No manual adjustments should be made to this protocol)

1) Tri-Planar Scout
2) IR-SPGR
3) Calibration Scan
4) Axial T2 Star
5) Axial Resting State fMRI (Eyes Open)
6) Axial T2 FSE
7) Axial DTI
8) Axial T2-FLAIR

After the completion of your qualification scans, your site will be required to upload images to LONI (see Appendix 5) using the DOD ADNI naming conventions detailed later in this section.

Any questions concerning MRI scanning related issues or site qualification scans please contact:
adnimri@mayo.edu

Any questions concerning sending MRI data to LONI please contact:
adni@loni.ucla.edu

B. Phantom Scan Instructions:

For site qualification, each site must scan the ADNI phantom using the electronically loaded DOD ADNI QC Phantom Sequences.

Note: This can be done prior to IRB approval

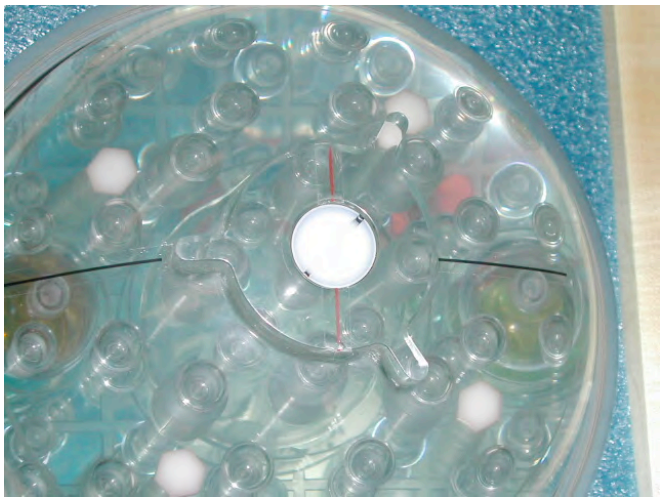
Please Note: Mayo QC will be supplying electronic protocols for installation by your local service engineer. This will ensure that you have the correct protocol for your MRI scanner. If you have any questions about this procedure please contact:
adnimri@mayo.edu
Use only the imported DOD ADNI sequences.

Phantom Positioning:

The following image shows the ADNI phantom placed in the appropriate position within the 8-channel coil. Achieving a reproducible position is a key element to the system performance analysis. The DOD ADNI QC phantom scans will be conducted each day a DOD ADNI subject(s) are imaged. The phantom should be placed in the coil with the alignment markers facing upward and the serial number SN XXXX positioned out of the bore as shown, along with alignment guides, will facilitate the reproducible positioning of your phantom.

ADNI phantom shown positioned inside of an 8-channel head coil.

Please note that your phantom has a base and positioning markers (in black and red, see image below). The phantom should be placed inside the head coil with the indicated "top" facing upwards. This orientation is due to space constraints within some coils and we would like to maintain a consistent orientation for all scanners across the DOD ADNI study. Please inspect the phantom and note the additional marks added to help you position your phantom. We have indicated the top of the phantom with red and black marks to aid with placement in the coil.



The top of the phantom and the alignment lines are indicated above. These markings should be used with the alignment lights on your scanner to position the phantom.

Please place the phantom in your head coil with the alignment marks facing up, and the phantom SN number (e.g. 9996) facing you, out of the bore (see the following picture). Furthermore, try to align the center of the phantom with the center of the coil. Use the alignment lights on your scanner to position the phantom into the center of the magnet.

The phantom is shown in the correct position, with the Serial Number (SN 9999) positioned forward and reading correctly from right to left. This will be the typical scanning position for your phantom

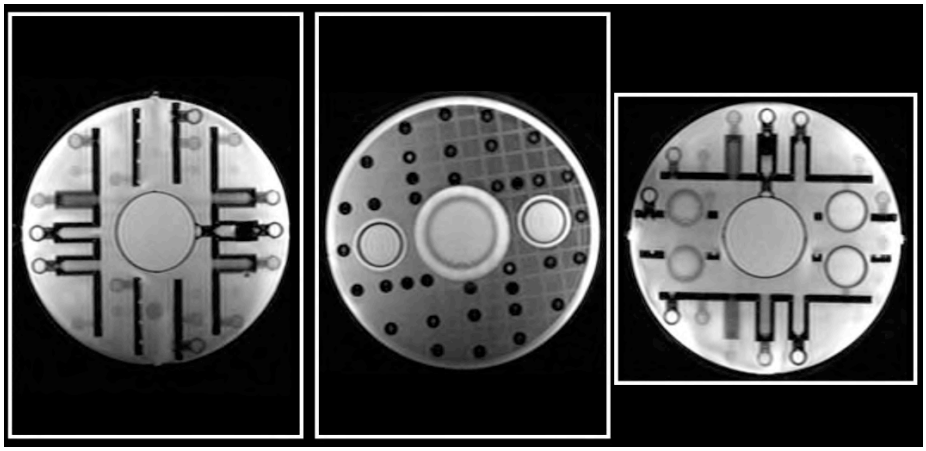
Phantom Scan Protocol:

Scan the phantom using the entire electronically loaded DOD ADNI QC Phantom protocol.

Phantom Scan Protocol:
1) Localizer
2) Calibration/Reference Scan (if applicable))
3) QC Phantom IR-SPGR (Accelerated)

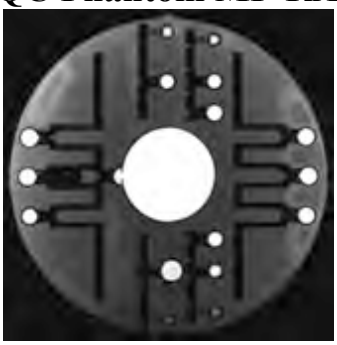
1. Localizer

3 Plane Localizer.



Example – Place FOV to cover entire phantom.

2. QC Phantom MP-RAGE/IR-SPGR (Accelerated)



Example

Data Transfer:

Please upload all the DOD ADNI QC phantom sequences acquired for the phantom scan to the LONI website as detailed in Appendix 5.

Phantom Naming:

1. **DOD ADNI Phantom Naming Convention *(entered during LONI upload)*:**

For the upload to LONI, phantom scans should follow the naming convention:

XXX_P_YYYY

X=Site#/ P=Phantom/Y=Phantom#

For example, each phantom scan from site 007 should be coded:

007_P_9999

2. **De-identification**

As part of the upload process to LONI, all the information entered into the scanner will be removed and replaced with the information entered during the LONI upload procedure. For this reason, you are encouraged to enter the phantom scan information into the scanner following standard local practice. However if your sites permits you can use the above naming convention as the subject ID that is entered in the scanner as well.

Phantom Scan Results:

Mayo QC will examine the phantom data, perform automated structural analysis on to determine gradient performance, check the image headers to determine if the correct parameters have been met and assure there are no other underlying problems with the scanning session. When finished, an email will be sent to your site notifying you of the results.

C. Human Volunteer Scan Instructions

1. ***After*** your site has received institutional IRB approval for the DOD ADNI protocol, a human volunteer must be scanned using the electronically loaded DOD ADNI protocol at 3T.

2. The volunteer should be consented by the study coordinator.

3. Since the data will be de-identified during the upload process to LONI, please enter the volunteer's information into the scanner following standard local practice.

4. Please scan the volunteer using the instructions outlined in "MRI Pre-Scan Procedures" addressed in section IV of this manual. It is crucial to follow the appropriate pre-scan procedures, subject positioning guidelines, and DOD ADNI sequences.

Human Scan Protocol:
(All scans are performed in straight orthogonal planes -- Sagittal or Axial)
(No manual adjustments should be made to this protocol)

1) Tri-Planar Scout
2) IR-SPGR
3) Calibration Scan
4) Axial T2 Star
5) Axial Resting State fMRI (Eyes Open)
6) Axial T2 FSE
7) Axial DTI
8): Axial T2-FLAIR

Data Transfer:
Please upload all the sequences acquired for the volunteer scan to the LONI website as detailed in Appendix 5.

D. Naming Convention Instructions

1. **DOD ADNI Volunteer Naming Convention:** ***(entered during LONI upload):***

   Volunteer scans should follow the naming convention:
   XXX_V_YYYY (X=Site#/ V=Volunteer#/Y=Vol#

   For example, each volunteer scan from site 007 should be coded:
   007_V_0001

2. **DOD ADNI Human Subject Convention:** ***(entered during LONI upload):***

   For subject scans, the naming convention will NOT include a site identifier, rather only the 7-digit subject ID will be used when uploading scans to LONI.

   In the ADCS EDC web portal, the SCRNO will equal SSSSSSS
   [S = seven digits subject ID]
   The seven digit subject ID will automatically append CS at the end of the ID to identify this is a clinic site participant

   For example, a scan from a study participant referred to site 007 would be coded:
   0001204 - CS

   However, when the scan is uploaded to LONI only the 7-digit subject ID portion of the ID should be used.

3. **De-identification** - As part of the upload process to LONI, all the information entered into the scanner will be removed and replaced with the information entered during the LONI upload procedure. For this reason, you are encouraged to enter the volunteer scan information into the scanner following standard local practice. However if your sites permits you can use the above naming convention as the subject ID that is entered in the scanner as well.

Human Volunteer Scan Results:
The Mayo QC team will perform a quality control check on the volunteer scan data. Mayo QC will determine if the correct parameters have been met and assure there are no other underlying problems seen during the scanning of this session. When finished, an email will be sent to your site notifying you of the results. In addition, an email will be sent to the selected contact list for your site notifying them your site has been approved and is ready to scan subjects.

Anticipation of Hardware Upgrades:
The Mayo QC team requires notification prior to any software and/or hardware upgrades for any scanner involved in the ADNI imaging study.

ADNIMRI@Mayo.edu

Depending on the impact of the upgrade the site may be required to scan a phantom and/or volunteer prior to continued scanning.

IV. MRI Subject Pre-Scan Procedures

A. Subject Pre-screening

1. All subjects should have been screened by the study coordinator for standard MRI contraindications. (A copy of the pre-screen form is available in Appendix 1) However, subjects must be re-screened for MRI contraindications immediately before the MRI scan using your 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.

2. Sedation during the Screening MRI scan is not offered for this protocol. Subjects that are uncomfortable with MRI scans should not be included in this study. If you have a subject who is uncomfortable with MRI and refuses to complete the scan without sedation, please contact the referring center and notify the study coordinator. Exceptions may be granted on a case-by-case basis by the clinical core to allow the use of sedatives for MR scans at visits **after** screening.

B. Subject Safety and Monitoring

1. All sites should follow the standard subject consent protocols as approved by your local IRB. Explain the scan procedure to the subject so that they know what to expect during the MRI.

2. Provide the subject with the opportunity to use the restroom before the scan begins.

3. Please use universal MRI safety precautions. Make sure that subject 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 (Please refer to Appendix 1 Pre-Screening Form).

4. Please use standard local practice for monitoring the subject during the scan. These may include devices to monitor pulse and O_2 levels.

C. Subject Positioning

1. Proper subject positioning is crucial for successful reproduction of serial MRI exams. Therefore, it is important that each subject is positioned in the same manner for each and every MRI exam.

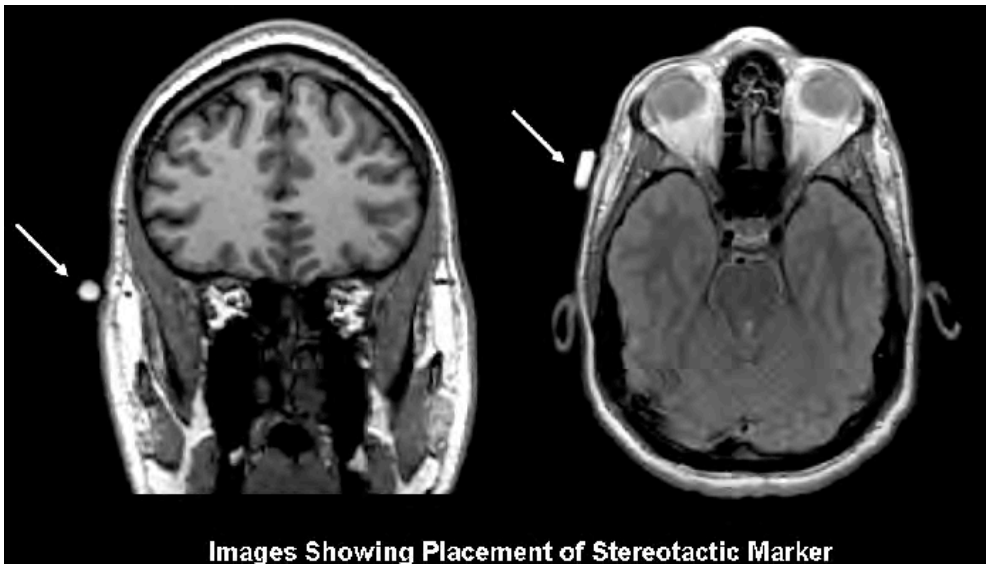
2. Please follow the procedures below for positioning the subject in the head coil:

    - Place clean sheet on scanner table and coil cradle.

    - Besides standard room exclusions ensure the subject 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.

    - **Tape stereotactic marker (vitamin E or fish oil capsule) on the subjects' right temple (RT).**



Images Showing Placement of Stereotactic Marker

- Provide each subject with ear protection.

- Position the subject 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 subject should also be well supported in the head coil to minimize movement. Motion artifacts may result in data rejection and request for a re-scan in many cases.

- 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 subject 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 on the subject's nasion *(directly between the eyebrows)* at every scanning session.**

Please Note:

- It is extremely important that the subject is positioned in the same manner, at the nasion, for the Screening MRI exam and for all the subsequent MRI visits.

- It is imperative that the subject positioning procedures are followed exactly for all follow-up exams for a particular subject to ensure consistent imaging of the brain.

- If a deviation from these instructions is required to accommodate a subject, the MRI technologist must note this on the MRI Scan Form and refer to these notes during the follow-up exam.

- Center the head coil over the subject's head, making sure the subject is high enough in the coil to prevent signal loss at the inferior aspect of the brain.

- Offer each subject a panic button in case of emergencies or claustrophobia if common local practice at your facility (for example, a squeeze ball alarm.)

- Remind subject to hold as still as possible and advance subject to the iso-center of the scanning bore.

V. MRI Subject Scan Protocol

DOD ADNI Subject Scanning Session Includes:

1) Tri-Planar Scout
2) IR-SPGR
3) Calibration Scan
4) Axial T2 Star
5) Axial Resting State fMRI (Eyes Open)
6) Axial T2 FSE
7) Axial DTI
8): Axial T2-FLAIR

Then following the subject scan, please scan the ADNI Phantom as a new exam:

- Localizer Scan
- Calibration Scan
- QC Phantom IR-SPGR (Accelerated)

The Mayo QC team will check all imaging parameters to assure the correct sequence was used. If the electronically loaded DOD ADNI sequence is not used to scan a subject, the scan will be excluded and the subject must be re-scanned with the correct DOD ADNI sequences.

A. MRI Scan Information Form

1. The "MRI Scan Information Form" should be completed at the time of acquisition for every DOD ADNI subject. A copy of the MRI worksheet is included in Appendix 2.

2. The study coordinator at the referral site should complete the top section of the MRI Scan Worksheet. If this section is incomplete, please contact the study coordinator for the information.

3. The MRI technologist should complete the remainder of the form during the scan. Please be sure to indicate if each sequence has been completed and note any problems or modifications to the protocol in the appropriate sections. Also, note if data transfer, archive, and local copy for clinical reads have been completed.

4. Please complete the form in full and transfer to the study coordinator at the referral site. The study coordinator will upload the information into the DOD ADNI database and this will be linked with the subjects' MRI data. Please keep a copy on site for your records.

5. To report an incident regarding the MRI sequences please email: ADNIMRI@mayo.edu

6. To report an incident about a specific subject please contact your study coordinator.

B. Entering Subject Information into the scanner

1. Please enter the subject's information into the scanner following your standard local practice. This will assure the scan is formatted for your local archival system. When data are uploaded to LONI the scan header will be de-identified and rendered HIPAA compliant. Data will be identified at the LONI site by subject code only. The subject code will be entered manually at the time of data transmission to LONI.

C. Scanning Sequences

#1: 3 Plane Localizer:

1. A quick acquisition in 3 orthogonal planes for anatomical orientation. Multiple slices acquired in the middle of each plane (sagittal, coronal, transverse). The head should be centered laterally along the inter-hemispheric fissure and centered on the thalamus for the anterior/posterior and superior/inferior planes. Please use the images below as reference when determining if the subject is positioned properly.

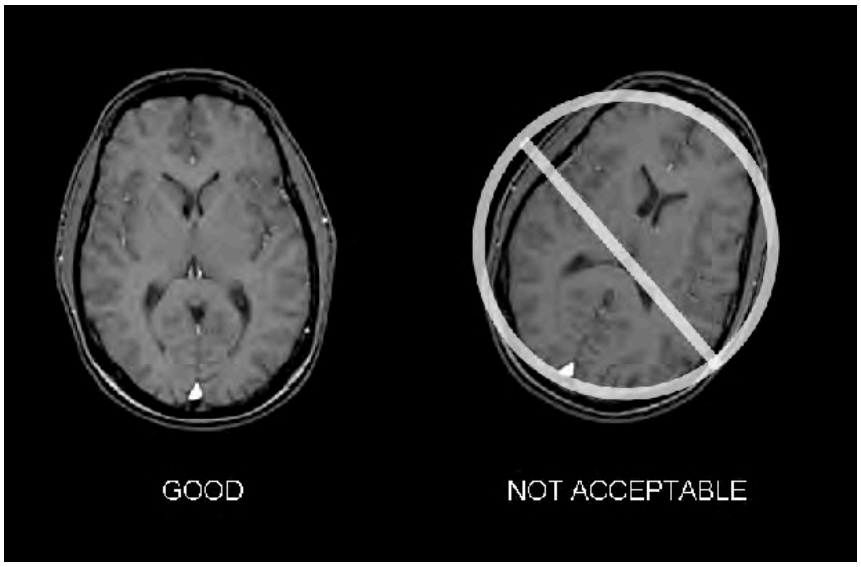
2. Proper placement in the head coil is crucial because scans are acquired in straight orthogonal planes. (Oblique scans are not allowed).

3. If the subject is not positioned properly please adjust the subject in the head coil and re-scout. Continue repositioning and scouting until the subject is correctly centered in the head coil.

Example:

Box A – Axial image. FOV placed in center to avoid side-to-side wrap.
Box B – Sagittal image. FOV placed anterior to avoid nose wrap.
Box C – Coronal image. FOV placed to assure top of the brain is covered.

Make sure subject is aligned correctly in the head coil and is not rotated. Their head should be as straight as possible in the coil. Please adjust the subject if necessary.



The head should be centered laterally along the inter-hemispheric fissure. Proper placement in the head coil is crucial because scans are acquired straight, not in an oblique orientation.

Please Note:

- It is mandatory that the DOD ADNI acquisition protocols electronically imported to your MRI be used for all sequences at the Screening MRI exam and for all the subsequent MRI visits unless otherwise directed by the coordinating center.
- Failure to use the same sequence at the time of Screening and all subsequent visits will result in the request for a rescan of the subject.
- It is mandatory that the DOD ADNI qualified scanner be used for all **subjects** in the DOD ADNI study.
- Failure to use the DOD ADNI qualified scanner for all **subjects** in the DOD ADNI Study will result in the request for a rescan of the subject.

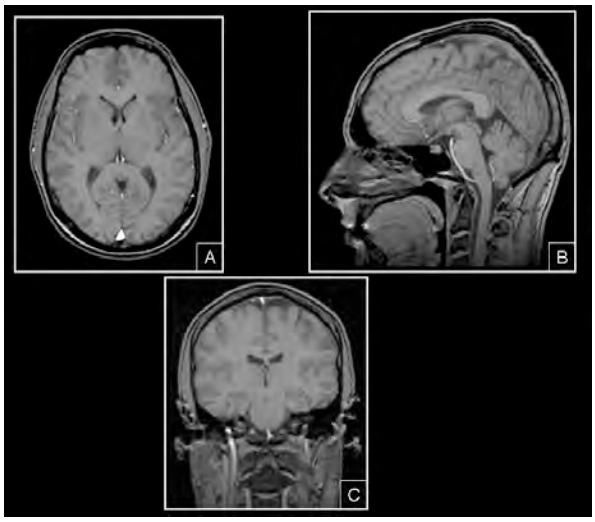
#2: 3D IR-SPGR:
Example:

1. Orientation. **<u>Straight</u>** sagittal. Slices will be prescribed from left to right. ***<u>DO NOT</u>*** oblique the scanning FOV to compensate for subject held tilt.

2. Positioning:
   Use the tri-planar scout to position the acquisition box. Make sure to get full head coverage**. Studies that do not contain the whole brain and skull cannot be processed.** The skull must be fully included superiorly and laterally. The entire cerebellum should be included inferiorly. **In the anterior/posterior plane please position so that the nose is also be included otherwise image folding into the back of the brain and may result and the exam may not be usable for the study**. Note: Images where the nose wraps to the back of the FOV, but is not impinging on the brain is acceptable.

   Please see the images below and use as a guide to correctly position the acquisition box.

   Example of 3 Plane Localizer for MP-RAGE FOV Placements



A – Axial image. FOV placed in center to avoid side-to-side wrap.

B – Sagittal image. FOV placed anterior to avoid nose wrap.

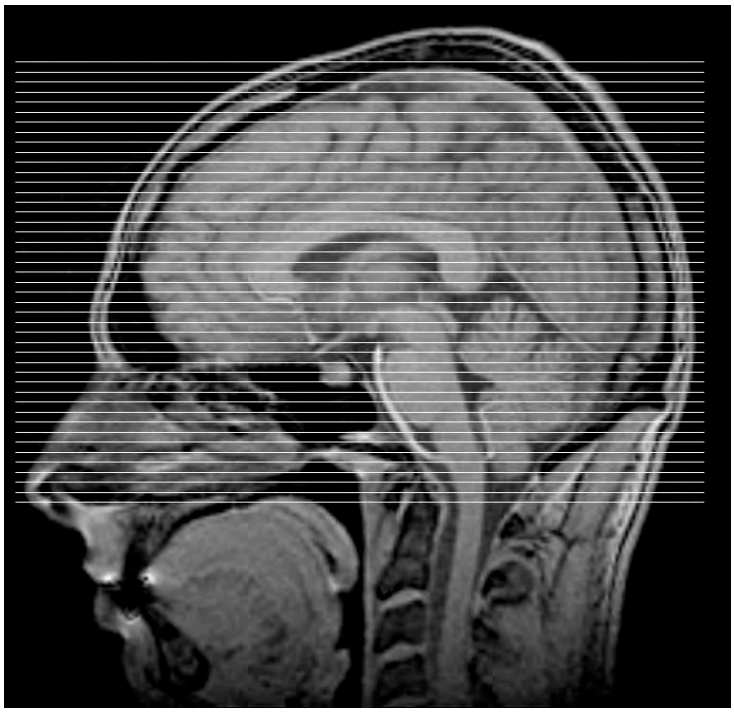
C – Coronal image. FOV placed to assure top of the brain is covered.

Positioning for all Axial Scans:

1. Orientation: **Straight** Axial. Prescribe slices inferior to superior.

DO NOT Oblique Scans.

2. Positioning: Position on mid-sagittal slice from tri-planar scout. Make sure to get full BRAIN coverage whenever possible. The acquisition stack should be placed just above the most superior point in the brain and should fully cover the cerebellum as well as all brain in the lateral and the anterior to posterior planes. If extra transverse slices are required to achieve this coverage please acquire those slices.



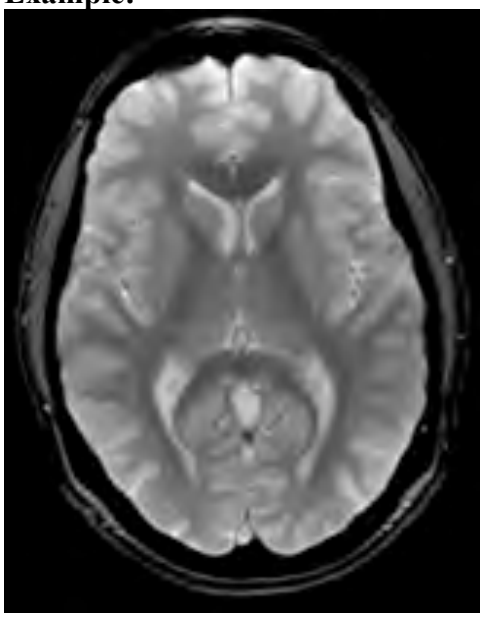
***** DO NOT oblique the scanning slices*** to compensate for subject held tilt. Scan as only straight Axials.

#3: Calibration:

MRI scanners provide automated adjustment procedures Calibration/RF coil tuning and frequency adjustments after the subject is positioned in the magnet. Follow the adjustment procedures provided by your manufacturer. The calibration scan included in the DOD ADNI protocol is a very large amount of axial slices to include a large FOV measure of the entire scanning volume. Please center the FOV to include several slices above the head and below the cerebellum. No other changes are needed.

#4: Axial T2-Star:

Example:

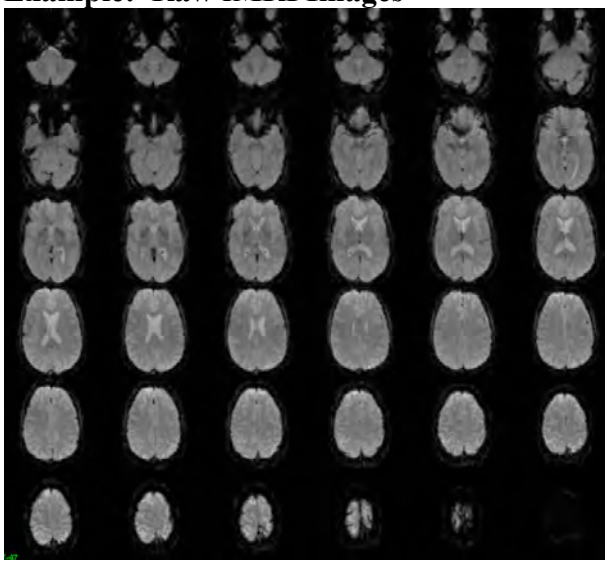


Orientation: Straight Axial. Prescribe slices inferior to superior. ** *DO NOT* oblique the scanning slices to compensate for subject held tilt. Scan as straight Axials. If extra transverse slices are required to achieve this coverage please acquire those slices.

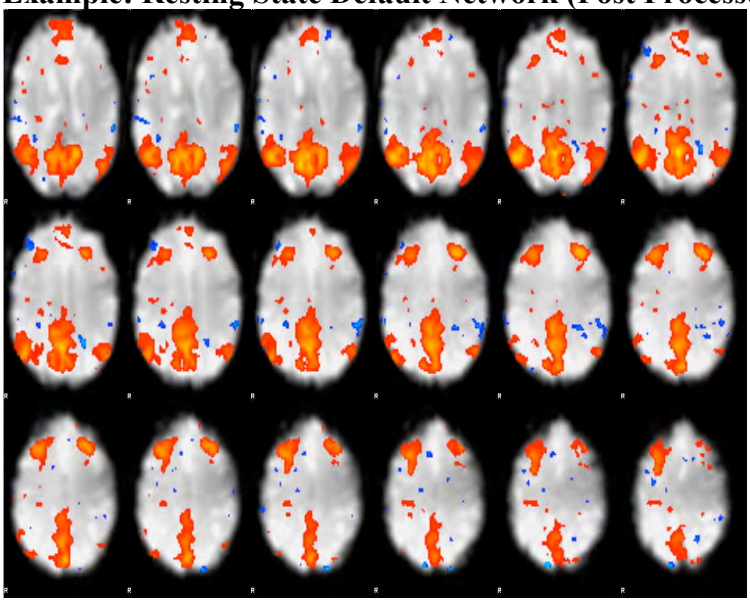
#5: Axial Resting State fMRI (EYES OPEN):

(Subject should have eyes OPEN)

Example: Raw fMRI Images



Example: Resting State Default Network (Post Processed Image)



1. Orientation: Straight Axial **--** DO NOT Oblique Scans.

2. Subject Instruction: **Please instruct the subject to keep their eyes open during the entire scan.** You can instruct them to focus on a point on the mirror or scanner. Also remind the subjects of the importance of holding their head still for the entire scan.

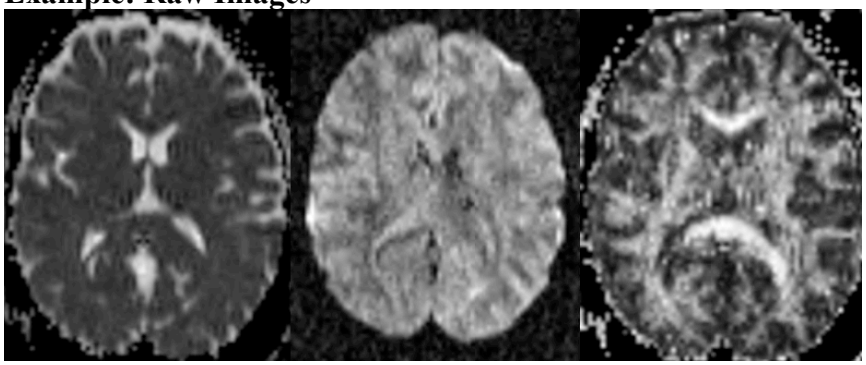
3. Positioning: Position on mid-sagittal slice from tri-planar scout. **The acquisition stack should be placed just above the most superior point in the brain and should cover the cerebellum if possible.**

#6 Axial T2 FSE:

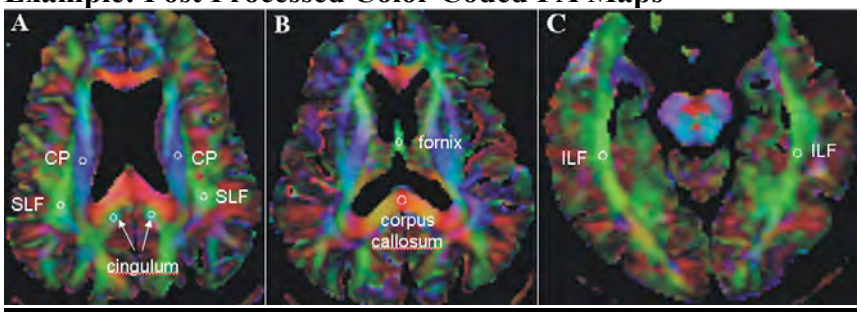
Orientation: Straight Axial. Prescribe slices inferior to superior. ** *DO NOT* oblique the scanning slices to compensate for subject held tilt. Scan as straight Axials.

#7: Axial DTI (Diffusion Tensor Imaging):

Example: Raw Images



Example: Post Processed Color Coded FA Maps

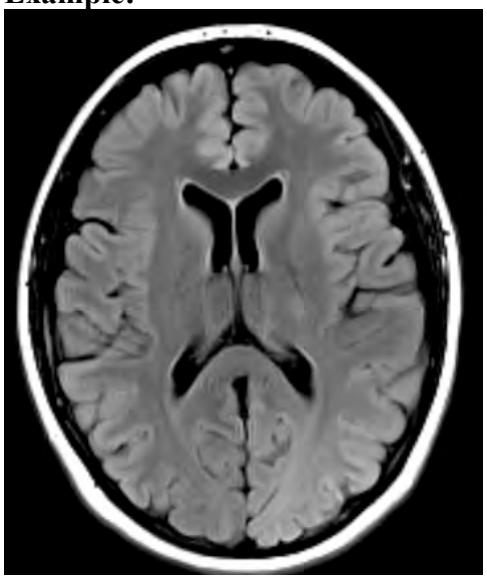


From Kantarci et al, submitted

Orientation: Straight Axial. Prescribe the 3D Slab inferior to superior. ** *DO NOT* oblique the slab to compensate for subject held tilt. Scan as straight axial.

#8: Axial T2-FLAIR:

Example:



Orientation: Straight Axial. Prescribe slices inferior to superior. ** *DO NOT* oblique the scanning slices to compensate for subject held tilt. Scan as straight Axials.

VI. MRI Subject Scan Procedures

A. Scan Discontinuation

1. If the subject 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 subject still does not want to complete the scan, then the MRI should be abandoned and noted as incomplete on the DOD ADNI 3T MRI Scan Worksheet. The comments sections should include the reason the subject was unable to complete the MRI.

B. Clinical Reads

1. **Every subject in the DOD ADNI Study *must* receive a clinical read by an on-site radiologist at each MRI facility.** The clinical read should follow standard local practice and a clinical dictation of the read should be transferred to the study coordinator at the referral site.
2. Clinical reads will **NOT** be provided by Mayo QC or LONI.

C. Archive Procedures

1. Every MRI (both human and phantom) for the DOD ADNI Study must be archived locally at the MRI facility following standard local practice in addition to the data transfer to LONI immediately after the MRI scan. Additional data transfers or copies will be requested by the coordinating center in the event that a data transfer is interrupted or incomplete. Possible MRI archive mediums include:
    - Optical Disk
    - PACS
    - CD or DVD
    - USB

D. Request for Repeat MRI Scans

1. Reasons for MRI Repeats:
    a. A request for a repeat MRI may be required in the event that the scans are found to be unacceptable due to subject motion or an incomplete MRI acquisition. Your site will be asked to schedule a repeat study.

    b. Mayo QC will check all DOD ADNI scans for protocol compliance. Repeat exams may also be required if the incorrect scan sequence, orientation, or angulations are used. It is imperative to use the DOD ADNI approved acquisition sequence with every DOD ADNI subject. Scans with image degradation due to the incorrect scan sequence, orientation, or angulations will **NOT** be reimbursed. Re-scans will be reimbursed if the correct scan sequence, orientation, and angulations were used.

2. Procedures for MRI Repeats:
    a. Repeat MRI scans should be performed as quickly as possible. The coordinating center for the DOD ADNI Study will contact the referral site as well as the MRI facility requesting a repeat MRI. Detailed information regarding the reason for the repeat as well as suggestions for improvement will be communicated to both sites.

VII. On Going Quality Control and Post-Subject Phantom Scanning Instructions

To ensure scanner stability and scan quality throughout the DOD ADNI Study, each site is **required** to perform *on going* quality control scans on the ADNI phantom using the DOD ADNI QC Phantom protocol each day a subject is scanned. If multiple subjects are scanned on a single day, only one phantom scan needs to be acquired

IMPORTANT: If a site fails to perform these phantom scans and they have not been performed within 24 hours, DOD ADNI will not reimburse the subject scan until received.

A. On Going Quality Control (QC) Phantom Scanning Instructions

For on-going quality control and post processing image analysis, each site must scan the specially designed ADNI phantom using the electronically loaded DOD ADNI QC protocols **each day a subject is scanned.**

On Going QC Phantom Scan Protocol:

Phantom Scan Protocol:
1) Localizer
2) Calibration/Reference Scan (if applicable))
3) QC Phantom IR-SPGR (Accelerated)

Please follow the phantom positing procedures indicated earlier in the manual.

Due to its small base, please store your phantom in the wooden box that it came in. This will ensure that the phantom does not roll of its base and fall when it is not being used.

Phantom Storage:

B. Phantom Naming:

1. **DOD ADNI Phantom Naming Convention *(entered during LONI upload)*:**

   For the upload to LONI, phantom scans should follow the naming convention:
   XXX_P_YYYY
   X=Site#/ P=Phantom/Y=Phantom#

   For example, each phantom scan from site 007 should be coded:
   007_P_9999

2. **De-identification** - As part of the upload process to LONI, all the information entered into the scanner will be removed and replaced with the information entered during the LONI upload procedure. For this reason, you are encouraged to enter the phantom scan information into the scanner following standard local practice.

C. Data Transfer:

Each site will send the phantom data (along with the subject data) to LONI within 24 hours after the completion of the scan as detailed in Appendix 5.

D. Measurements:

The Mayo QC team will perform the following measurements on the phantom data: Gradient Linearity Measurements, Signal to Noise measurements, Image contrast, Inhomogeneity, and RF Power measurements.

E. Phantom Results and Site Notification:

Mayo QC will examine each phantom data set to ensure that there are no underlying problems with the scanning session, and that the scanner has not drifted out of specification. When finished, if there is an issue that needs to be addressed, an email will be sent to your site notifying you of the problem.

VIII. Appendices

Appendix 1: MRI Pre-Screening Form

The following is an example of the form subjects complete with the study coordinator prior to their MRI scans. The study coordinator should notify the MRI site if the subject has indicated yes for any items that may pose a risk to the subject (i.e. internal metal) during the MRI. This form should not be a substitute for your standard pre-screening form.

Date _____/_____/___

Subject ID _____

Please check Yes/No for each of the following:

☐ Yes ☐ No Previous MRI scan

Exclusionary Items:

☐ Yes ☐ No Cardiac pacemaker / defibrillator
☐ Yes ☐ No Aneurysm or aortic clip(s)
☐ Yes ☐ No Neurostimulator
☐ Yes ☐ No Cochlear, otologic, or ear implant

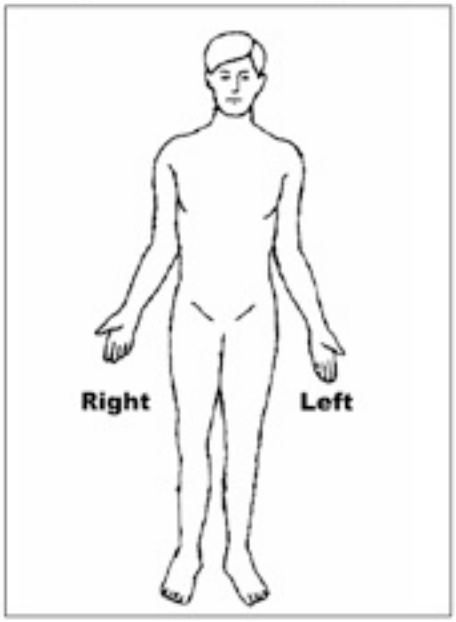
Please Inform MRI Center:

☐ Yes ☐ No Prosthesis or implant
☐ Yes ☐ No Artificial limb or joint
☐ Yes ☐ No Insulin or infusion pump
☐ Yes ☐ No Bone growth / fusion stimulator
☐ Yes ☐ No Carotid artery vascular clamp
☐ Yes ☐ No Electrodes (on body, head, or brain)
☐ Yes ☐ No Stents, filters, or coils (intravascular)
☐ Yes ☐ No Shunt (spinal or intraventricular)
☐ Yes ☐ No Vascular access port and / or catheter
☐ Yes ☐ No Tattooed makeup (eyeliner, lips, etc.)
☐ Yes ☐ No Body piercing(s)
☐ Yes ☐ No Any metal fragments or shrapnel (current or removed)
☐ Yes ☐ No Internal pacing wires
☐ Yes ☐ No Metal or wire mesh implants
☐ Yes ☐ No Bone / joint pin, screw nail, wire, plate
☐ Yes ☐ No Breathing disorder
☐ Yes ☐ No Claustrophobia
☐ Yes ☐ No Hearing aid (***Remove before MRI***)
☐ Yes ☐ No Dentures (***Remove before MRI***)

If answers below are yes, please explain below

☐ Yes ☐ No Worked extensively with metal (grinding, etc.)
☐ Yes ☐ No A history of seizures continuing to present

Please mark on the figure below the location of any implant or metal inside or on your body



Remove all metallic objects prior to your MRI examination

Explanation _____

_____ _____
Signature of subject or subject's representative *Name of Representative*

_____ Date _____/_____/_____
Signature of person administering screening form

Date _____/_____/_____

Appendix 2: MRI Scan Information Form

- The "MRI Scan Information Form" should be completed at the time of acquisition for every DOD ADNI subject. A copy of the MRI worksheet follows.

- The study coordinator at the referral site should complete the top section of the form. If this section is incomplete, please contact the study coordinator for the information.

- The MRI technologist should complete the remainder of the form during the scan. Please be sure to indicate if each sequence has been completed and note any problems or modifications to the protocol in the appropriate sections. Also, note if data transfer, archive, and local copy for clinical reads have also been completed.

- Please complete the form in full and transfer to the study coordinator at the referral site. Please keep a copy on site for your records.

Alzheimer's Disease Cooperative Study

ADCS

3T MRI Scan Information

Visit: Screening MRI

DOD ADNI PARTICIPANT NUMBER | SITE ID | EXAMINER INITIALS | EXAMINATION DATE (MONTH / DAY / YEAR)

To be completed by Study Coordinator:

Study Coordinator Name: _____

Telephone #: _____

Scheduled Date: MONTH / DAY / YEAR

DOD ADNI Participant Initials:

To be completed by MRI Technologist *(If section above is incomplete please contact study coordinator for participant information)*:

NOTE: Every visit should have **ORIGINAL** scan data entered before any rescan data is entered.

Was the scan conducted? ☐ Yes ☐ No

If No, please provide reason why the scan was not conducted:

☐ Illness ☐ Participant unavailable ☐ Participant unwilling ☐ Administrative problems

☐ Withdrawn consent ☐ Other (specify): _____

Important: It is mandatory that the DOD ADNI site qualified scanner be used for ALL participants in the study. Do NOT adjust protocol values.

MRI Operator Initials

Scan Date MONTH / DAY / YEAR

Was sedation medication consumed for use during MRI scan? (*Sedation medication is not allowed at screen.***)**

☐ Yes ☐ No

Please follow instructions in the DOD ADNI Technical Manual for positioning the participant in the head coil.

Placed Stereotactic Marker on the participant's (RT) temple? ☐ Yes ☐ No

Scan #1: Plane/Tri-Planar Scout (if available, otherwise use an axial scout): *Check participant positioning in the head coil, reposition and re-scout if necessary.*

Scout Completed? ☐ Yes ☐ No

Comments: _____

_____

Scan #2: <u>Straight</u> Sagittal 3D IR-SPGR: *DO NOT oblique the scanning FOV to compensate for participant held tilt. Position FOV to avoid nose wrapping into the back of the brain.*

IR-SPGR – Completed? ☐ Yes ☐ No

Comments: _____

_____

Alzheimer's Disease Cooperative Study

ADCS

3T MRI Scan Information

Visit: Screening MRI

DOD ADNI PARTICIPANT NUMBER

Scan #3: Calibration: *Please center the FOV to include several slices above the head and below the cerebellum.*

Calibration Completed?? ☐ Yes ☐ No

Comments: _____

_____

_____

Scan #4: Axial T2 Star:

Position Slices to cover below cerebellum through the top of the head. DO NOT oblique the scanning slices.

T2 Star Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Scan #5: Axial Resting State fMRI (Participant should have eyes OPEN):

Was the participant instructed to open their eyes? ☐ Yes ☐ No

Did the participant keep their eyes open? (MRI Tech: ask the participant right after the scan) ☐ Yes ☐ No

The acquisition stack should be placed just above the most superior point in the brain and should cover inferior as much as possible, if the cerebellum is not covered fully, that is acceptable. Instruct the participant prior to this scan that they should have their eyes open and to hold very still. DO NOT oblique the scanning slices.

fMRI Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Scan #6: Axial T2 FSE

Position Slices to cover below cerebellum through the top of the head. DO NOT oblique the scanning slices.

FSE Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Alzheimer's Disease Cooperative Study

ADCS

3T MRI Scan Information

Visit: Screening MRI

DOD ADNI PARTICIPANT NUMBER

Scan #7: Axial DTI Scan:

Position Slices to cover below cerebellum through the top of the head. DO NOT oblique the scanning slices.

DTI Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Scan #8: Axial T2 - FLAIR:

Position Slices to cover below cerebellum through the top of the head. DO NOT oblique the scanning slices.

FLAIR Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Scan #9: Phantom QC Scan(s): Position Slices to completely cover the phantom. DO NOT oblique the scanning slices. DOD ADNI phantom scan is required on the day of the DOD ADNI participant scan (only one phantom scan is needed even if there are multiple participants scanned on a single day.)

Phantom Completed? ☐ Yes ☐ No

Comments: _____

_____

_____

Participant Motion Problems: ☐ Yes ☐ No

Comments: _____

_____

_____

Scanner Malfunction: ☐ Yes ☐ No

Comments: _____

_____

_____

Alzheimer's Disease Cooperative Study

ADCS

3T MRI Scan Information

Visit: Screening MRI

DOD ADNI PARTICIPANT NUMBER

Other Protocol Variations: ☐ Yes ☐ No

Comments: _____

_____

_____

Was data transferred to LONI within 24 hours of scan?: ☐ Yes ☐ No

Transfer Date: MONTH (☐☐) DAY (☐☐) YEAR (☐☐☐☐)

Comments: _____

_____

_____

Data Archived Locally? (If No, please explain under comments.)

☐ Yes

Archive Medium:

- ☐ PACS
- ☐ CD/DVD
- ☐ MOD
- ☐ Other:

☐ No

Comments: _____

_____

_____

Was a Lumbar Puncture completed prior to the MRI scan? (To be completed by the Study Coordinator)

☐ Yes ☐ No

If Yes, What was the interval between LP and MRI?

☐ less than 6 hours	☐ 13-24 hours	☐ 49-72 hours
☐ 6-12 hours	☐ 25-48 hours	☐ more than 72 hours

Appendix 3: MRI Acquisition Summary

Please Note: Mayo QC will be supplying electronic DOD ADNI protocols for installation to your local service engineer for your MRI system. This will ensure that you have the correct protocol for your MRI scanner. If you have any questions about this procedure please contact:
ADNIMRI@Mayo.edu
Use only the imported DOD ADNI sequences
(Do NOT manually type in protocols)

DOD ADNI 3T QC Phantom Scan Protocol:

QC Phantom Scan Protocol:
1) Localizer
2) Calibration Scan
3) QC Phantom IR-SPGR (Accelerated)

DOD ADNI 3T Human Protocol:

(All scans are performed in straight orthogonal planes -- Sagittal or Axial)
(No manual adjustments should be made to this protocol)

Human Protocol:
(All scans are performed in straight orthogonal planes -- Sagittal or Axial)
(No manual adjustments should be made to this protocol)

1) Tri-Planar Scout
2) IR-SPGR
3) Calibration Scan
4) Axial T2 Star
5) Axial Resting State fMRI (Eyes Open)
6) Axial T2 FSE
7) Axial DTI
8): Axial T2-FLAIR

Appendix 4: FAQ's -- Frequently Asked Questions:

Q – My subject's head is tilted quite a bit. Can I oblique the scans then?
A – No, do not oblique the scans, we can deal with the subjects head being tilted more easily than we can with scans that were acquired obliquely.

Q – I forgot to put the marker on the subject. Do we need to rescan?
A – No, that will not be a reason for re-scan, please just try to remember next time.

Q – What is the phantom filled with?
A – Mostly distilled water and some anti mold ingredients. If you notice your water level is getting low, please top off with distilled water. Distilled water acts differently when imaged than tap water, so please make sure you are using distilled water.

Q – Can I scan the phantom in the same exam as the subject?
A – No please, start a new exam and name the phantom with the correct ID. The phantom scans are handled differently than the subject scans. Starting a new exam gives that study a different unique identifier (UID) thus much easier to upload separately and store separately.

Q – I noticed some wrap on my image. Should I increase the FOV to compensate?
A – No, unless the wrap is affecting brain tissue you do not need to re-scan. If the wrap is affecting brain tissue please try to place the FOV to avoid wrap if possible.

Q – Should I append this scan to the previous scan in the PACs system.
N – Please do not append the sessions, it causes the exams all to have the same UID.

Q – Do I need to have the subject remove their dentures?
A – Yes, please have all your subjects remove their dentures to avoid artifact.

Q – I conducted MR scans for 2 ADNI2 subjects and 1 DOD ADNI subject today. Do I need to scan the phantom 3 times?
A – No you just need to scan the phantom once per day for those related studies. However you may need to upload the phantom data twice to LONI (for ADNI2 **and** for DOD ADNI site).

Q – I am having trouble with upload data to LONI, who do I contact?
A - adni@loni.ucla.edu

Q – The exam was already sent to LONI, do we need to keep a copy of it?
A – Yes, please keep a copy of all human AND QC phantom scans your site performs.

Q – Our scanner was upgraded, do I need to re-certify?
A – If it was a major upgrade (both software and hardware) the answer is yes. However, many minor upgrades do not need a full re-certification scan, just a phantom scan. In that case, we may just ask you run the QC phantom scans to make sure the pulse sequences are working.

Appendix 5: Data Transfer to LONI

Uploading MRI data to the Laboratory of Neuro Imaging (LONI)

Image Data Archive Instructions

CONTENTS:

A - Image Data Archive Overview

B - System Requirements

C - User Registration

D - IDA Log in

E - Archive Process Overview

F - Archive Instructions

G - Archiving Data in Batch

A - IMAGE DATA ARCHIVE OVERVIEW

The LONI Image Data Archive (IDA) provides an integrated environment for safely archiving, querying and visualizing neuroimaging data utilizing a web-browser interface. The archive protects data from unauthorized access while providing the ability to share data among collaborative investigators.

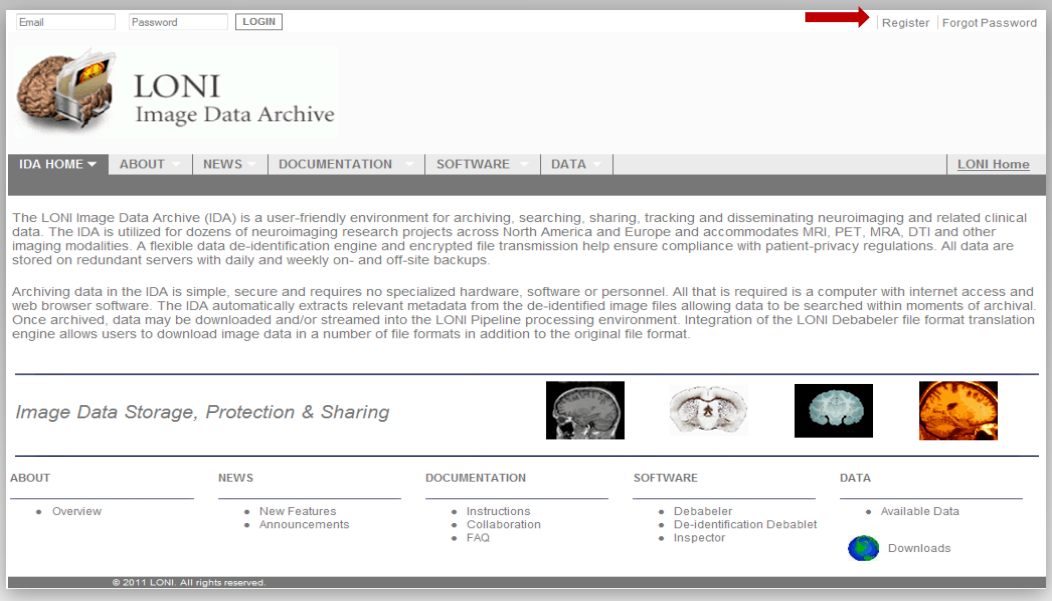
For questions or problems with the IDA please send email to adni@loni.ucla.edu

B - SYSTEM REQUIREMENTS

The IDA system requires a computer with Internet access, newer web browser software (IE, Netscape, Mozilla, Safari), Java Plug-in (Oracle/Sun version 1.5 or higher), and a valid user account.

C - USER REGISTRATION

If you do not have a user account, Click Register on the Image Data Archive Log-In page. https://ida.loni.ucla.edu.

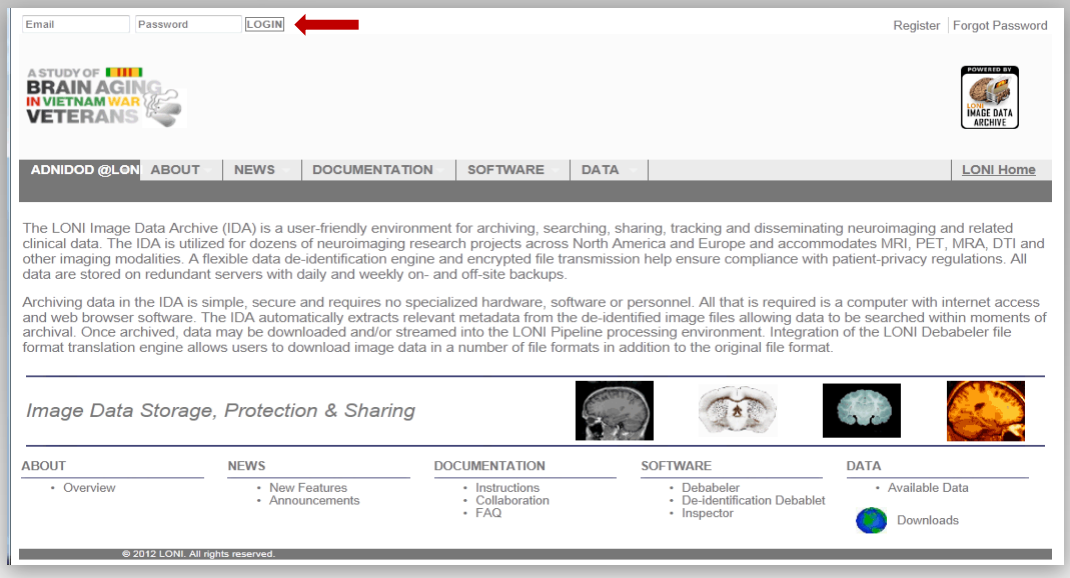


Complete the form to create a new account then click the REGISTER button.

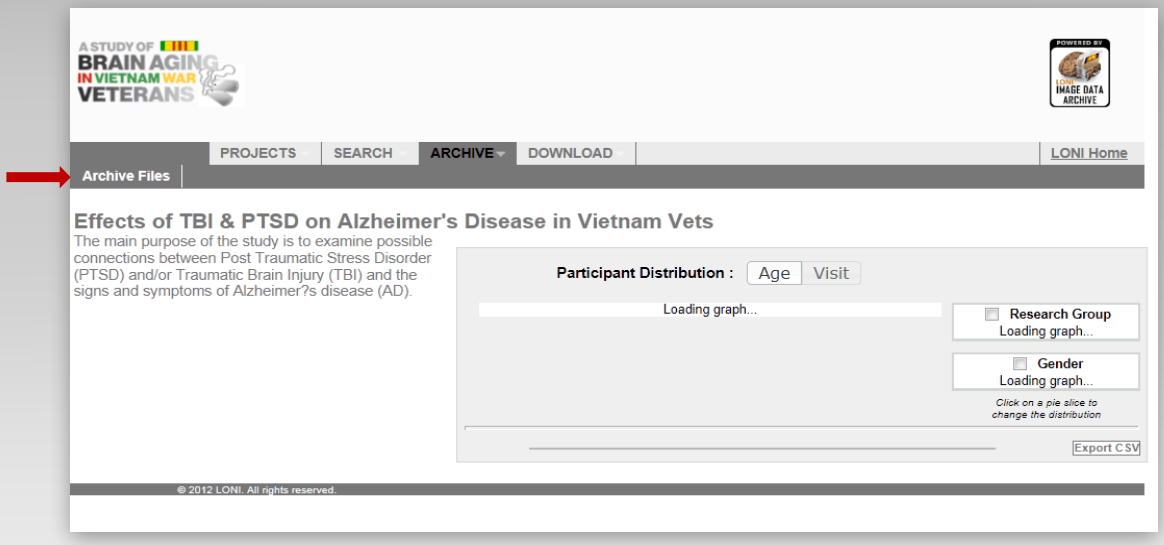
Once the registration process is complete, a confirmation email will be sent with a temporary password and login instructions.

D – IDA LOG IN

On the Log-in page at https://ida.loni.ucla.edu/login.jsp?project=ADNIDOD, provide your email address and then click Login. New users, please refer to the user registration section for instructions on how to register for a user account.



Select Archive Files from the ARCHIVE menu.



E – ARCHIVE PROCESS OVERVIEW

There are two steps in the archive process: de-identification and file transmission. The de-identification step removes or replaces potentially identifying subject information from image headers.

During the file transmission step, the de-identified files are securely transmitted to LONI and stored in the data archive.

SYSTEM REQUIREMENTS

The IDA system requires a computer with Internet access, newer web browser software (IE, Netscape, Mozilla, Safari), Java Plug-in (Oracle/Sun version 1.5 or higher), and a valid user account.

PROCESS

Following user authentication, the user chooses the data to be archived by selecting the directory where the data are located and chooses a directory where the de-identified files will be written. Next, a Java applet de-identifies the files, inserting the user-supplied subject identifier and removing or replacing other potentially identifying information. The user is given the opportunity to validate the de-identification results, prior to transmitting the images. Once the results of the de-identification process have been validated, the files are transmitted from the user's local computer to LONI. Upon arrival at LONI, the data are stored in a fault-tolerant storage area network and the database is populated with relevant metadata attributes.

The archive log in page is available from IDA Home page https://ida.loni.ucla.edu/login.jsp?project=ADNIDOD. Enter your email address and password then click the Sign-In button. New users, please refer to the user registration section for instructions on how to register as a user.

F - ARCHIVE INSTRUCTIONS

Use the Single Archive process to upload one or more files from a single subject.

PREREQUISITES

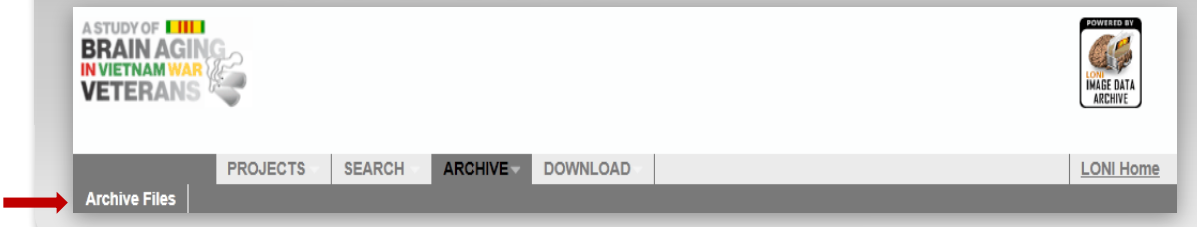
Place all image files for each subject within a single directory (source directory), which may contain subdirectories. The source directory must not contain multiple image formats.

Create an empty directory where the de-identified files will be written (target directory).

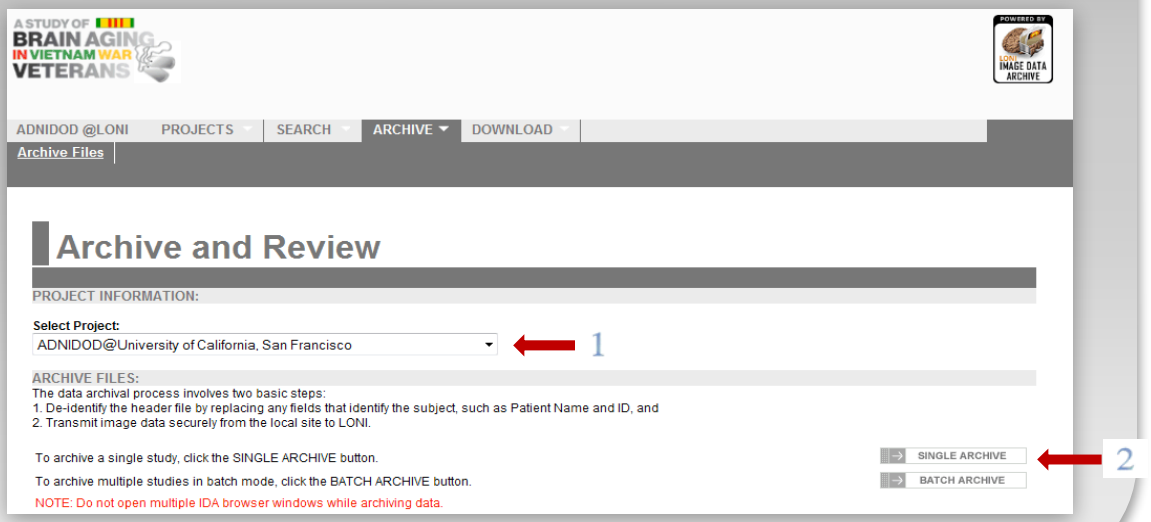
NOTE

- The browser window must remain open during the entire upload process. Closing the browser window cancels the upload.

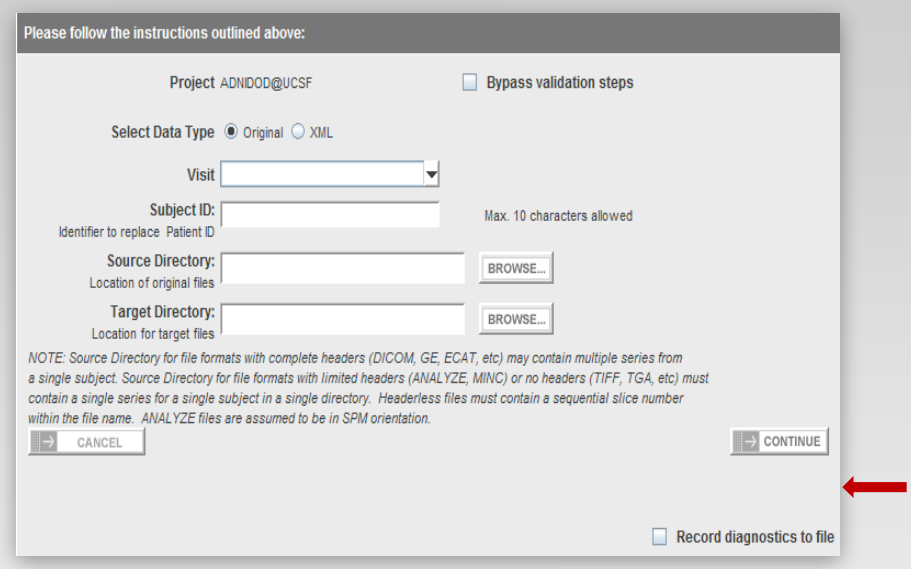
Choose Archive Files from the Archive menu.



- Select your Project/Site from the drop down menu (1).
- Click SINGLE ARCHIVE (2).

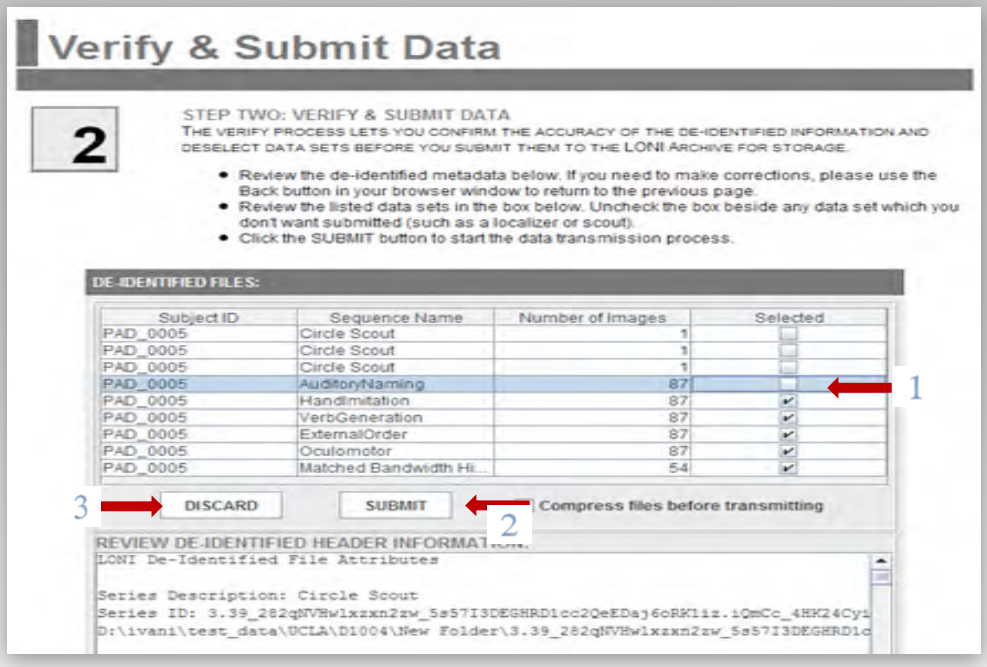


1. On the De-Identify page:
    - Select a Visit.
    - Provide a Subject ID.
    - Click Source Directory - Browse to find the directory which contains the file(s) to be uploaded or provide the directory path then click Select Source File Directory.
    - Repeat the process to select a Target Directory to contain the de-identified files.
    - To upload files without validating de-identification results, check the Bypass Validation Steps box (not recommended for first time users).
    - Click CONTINUE to begin the de-identification process.
    - To automatically record any issues during the archive process, check the box near Record diagnostics to file. You will be prompted to provide a location to store the diagnostics file. Note: this is an optional step.



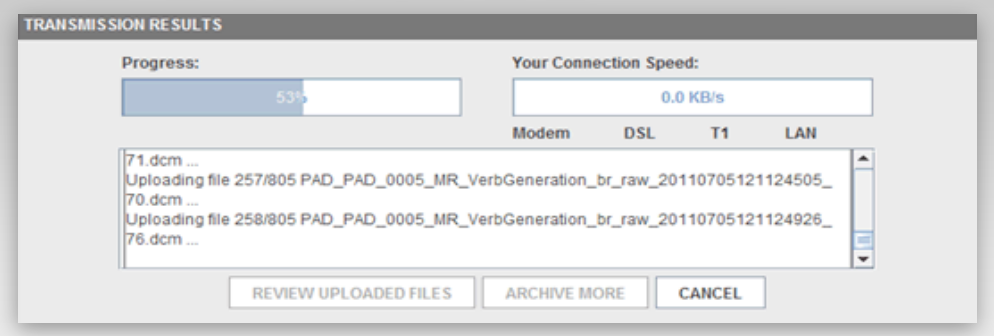
➢ When the de-identification step is complete, a list of de-identified files is shown along with the de-identified header information.

- To remove any images, uncheck the Selected box beside the image (1).
- Click SUBMIT to transmit the de-identified images (2).
- Choosing Discard cancels the upload and returns to the previous page (3).



- The progress bar shows the status of the file transmission step.

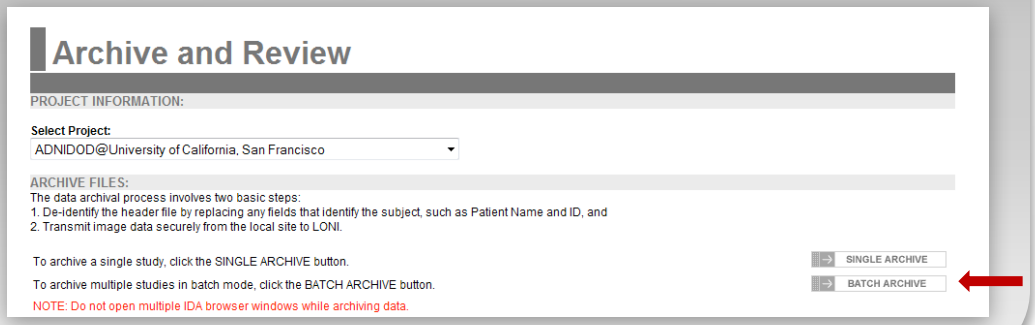
- Once the file transmission is complete, click REVIEW UPLOADED FILES to view the results of the archiving process
.
- Or click ARCHIVE MORE to upload more files.



G. ARCHIVING DATA IN BATCH

The Batch Archive process is similar to Single Archive, except that multiple subjects and image series can be submitted in a batch. Batches can be of the same or different file formats and modalities. However, users cannot review the results of the de-identification process prior to the batch upload

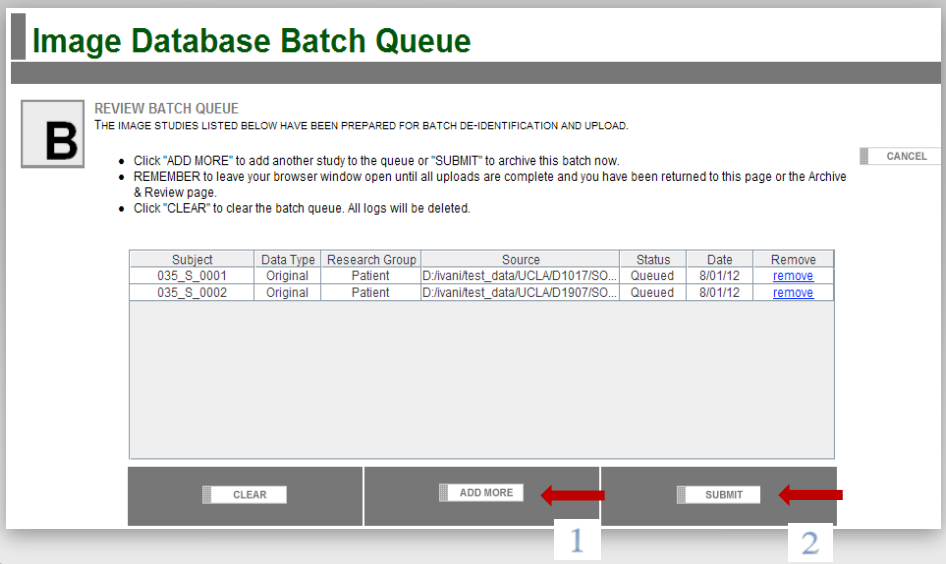
Click BATCH ARCHIVE on the Archive and Review page.



Follow the instructions on the Single Archive section.

On the Batch Queue page, click ADD MORE(1) to add more studies. Repeat this process for each series or subject to be archived.

Click SUBMIT(2) to de-identify and upload all files.



DETAILS:

- Once files are archived, click Review Uploaded Files to view a list of all the successfully archived images. Or click Archive More to upload more files