

Dominantly Inherited Alzheimer Network (DIAN) MRI Technical Procedures Manual

More information and imaging updates can be found at: http://nrg.wikispaces.com/DIAN+MRI_Updates

DIAN Study Background and Significance

Alzheimer disease (AD) is the most common cause of dementia and is an increasing public health problem. It is currently estimated to afflict 5 million people in the United States, with an expected increase to 13 million by the year 2050. AD leads to loss of memory, cognitive function, and ultimately independence. AD takes a heavy personal and financial toll on the patient and the family. Because of the severity and increasing prevalence of the disease in the population, it is urgent that better treatments be developed.

Currently, there are some approved medications that temporarily ameliorate symptoms, however, there are no disease modifying treatments. Disease modifying treatments will likely be most effective when given *before* the onset of permanent brain damage. However, by the time clinical diagnosis of AD is made, extensive neuronal loss has already occurred. Identifying the pathophysiologic changes that occur in AD *before* clinical onset is an ideal approach to diagnose those at risk and may provide a measure to study the effect of disease modifying treatments. The study of disease mechanisms that lead to AD in pre-symptomatic humans will likely yield new insights into the pathogenesis, diagnosis, and treatment of AD.

ADAD: The only identified deterministic factor for the development of AD is the presence of a mutation in one of three genes (*APP*, *PSEN1*, *PSEN2*) or duplication of *APP*. The most striking evidence in support of causative genetic factors is the existence of families in which the disease is inherited as fully penetrant autosomal dominant AD - ADAD. Fifty-percent of the people from these kindreds (mutation carriers) are destined to develop DAT, most of which are early onset (<60 years). ADAD is similar to the more common, later onset AD in many aspects of clinical presentation, pathologic changes, and biochemical changes. The discovery of ADAD-causing mutations has led to a significant increase of knowledge about AD through molecular biology studies and animal models. Most of the pre-clinical research in AD is based on the mutations that were discovered in ADAD pedigrees. The study of the underlying pathophysiology of ADAD through metabolism studies, biomarkers and imaging techniques will likely lead to further understanding of later onset AD.

While there are presently no proven treatments that delay the onset or prevent the progression of AD, many promising candidates have this potential. During the development and ultimate implementation of these therapies, it will be critically important to have biomarkers which will measure the effects of these treatments on the structure, function and biochemistry of the human brain. In order to establish a baseline and longitudinal dataset which describes the progression of ADAD from a preclinical through moderate stage of DAT, we propose to form the Dominantly Inherited Alzheimer Network (DIAN). DIAN will serve to determine the chronological changes in imaging, biomarkers, and psychometric tests in relation to clinical onset and progression, in a well characterized and uniformly studied group of ADAD individuals.

DIAN will study dominantly inherited AD in individuals for whom the diagnosis is certain (mutation carriers) in comparison with their non-carrier siblings, who serve as a naturally occurring control group. All DIAN participants will be assessed longitudinally with comprehensive and state-of-the-art clinical, cognitive, genetic, imaging, and biomarker protocols, and all data will be collected in a standard and uniform manner for entry into a central repository. This research database will be harmonized with other databases (ADNI; NACC) that use methods and protocols identical to DIAN, and will serve to promote data sharing within and without DIAN.

Over Years 01-06, sites will recruit, enroll, and follow individuals from ADAD kindreds to reach a total sample size of up to 400 individuals. We anticipate that the DIAN cohort will be about 80% presymptomatic, 15-20% symptomatic.

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General Information

The purpose of this manual is to further explain the MRI imaging component of the DIAN protocol. Standard procedures are needed to ensure consistency of data collection in this longitudinal study.

This manual contains information for study-site staff involved with the care of the study participants during the imaging procedures and those involved with scanning the study participants.

Contact Information

If you have any questions or concerns regarding MRI imaging study please contact:

DIAN-MRI@dian-info.org

If you have question regarding the scan uploading to the CNDA please contact:

cnda-help@dian-info.org

Site Qualification

Prior to any DIAN subjects being scanned at a particular site, that site must complete DIAN site qualification. Site qualification includes two different exams. The first, being a scan on the specially designed DIAN phantom with the electronically provided DIAN sequences loaded by your local service engineer or lead technologist. Secondly, your site will be asked to scan a human volunteer with the approved DIAN sequences loaded by your local service engineer. Mayo QC will review the phantom and human scans for the correct parameters, good image quality and scanner performance. If either scan does not pass Mayo QC review, your site will be asked to re-scan after making the suggested changes by the Mayo QC team. All MRI scans will be conducted on 3T scanners.

Phantom Quality Control Scan Protocol:

- 1) Localizer
- 2) QC Phantom Sagittal 3D Accelerated MPRAGE
- 3) QC Phantom Sagittal 3D Non - accelerated MPRAGE
- 4) QC Phantom Coronal 3D Non - accelerated MPRAGE

****(For Siemens Systems VB17 and Current Release Philips Systems The QC protocol will change to: QC Phantom Sagittal 3D Accelerated MPRAGE, QC Phantom Coronal 3D Non - accelerated MPRAGE and QC Phantom Axial Resting State fMRI.*

Human Volunteer Scan Protocol:

(No adjustments should be made to this protocol)

- 1) 3-Plane Localizer
- 2) Sagittal 3D Accelerated MPRAGE
- 3) Sagittal 3D Accelerated MPRAGE REPEAT
- 4) Axial T2 FLAIR
- 5) Axial Resting State fMRI - *(Subject should have eyes OPEN)*
- 6) Axial SWI or T2* Axial GRE
- 7) DIAN Suggested – DTI

After each scanning session, please upload the DICOM images to the Central Neuroimaging Data Archive (CNDA) using the DIAN naming conventions detailed later in this manual.

If you have question regarding these site qualification scans, please contact:

DIAN-MRI@dian-info.org

NOTE: The one MRI scanner that is qualified for DIAN at your site must be used for ALL subsequent subject scans during the DIAN study. If the same MRI scanner is not used, the scan will not be reimbursed, and the subject will need to be re-scanned on the DIAN qualified scanner.

Phantom Scan Instructions

For site qualification, each site must scan the provided DIAN or ADNI phantom using the electronically loaded DIAN QC Phantom protocols.

Note: This can be done prior to IRB approval.

Phantom Positioning:

The following image shows the phantom placed in the appropriate position within an 8-channel coil. Achieving a reproducible position is a key element to the system performance analysis that will be done bi monthly. The phantom should be placed in the coil with the alignment markers facing upward and the serial number SN XXXXX positioned out of the bore as shown, along with alignment guides, this will facilitate the reproducible positioning of your phantom.



DIAN 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. 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.

NOTE: The Mayo QC Team will be supplying electronic protocols (WIPs) for installation by your local service engineer, physicist, or lead technologist. This will ensure that you have the correct protocol for your MRI scanner.

If you have question regarding this procedure, please contact:

DIAN-MRI@dian-info.org

Use only the imported DIAN sequences.



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) is 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.



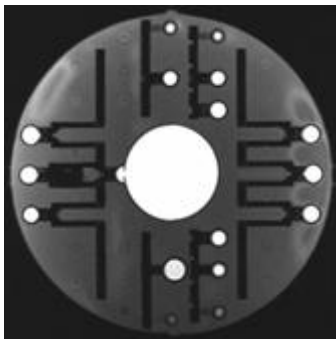
The phantom is shown in the correct position, with the Serial Number (SN 9999) positioned forward and reading correctly from right to left. This will be the typical scanning position for your phantom

Phantom Scan Protocol:

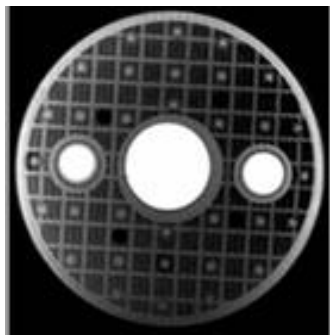
Scan the phantom using the electronically loaded DIAN QC Phantom protocols which include.

- 1) Localizer
- 2) QC Phantom Sagittal 3D Accelerated MPRAGE
- 3) QC Phantom Sagittal 3D Non - Accelerated MPRAGE
- 4) QC Phantom Coronal 3D Non - Accelerated MPRAGE

****(For Siemens Systems VB17 and Current Release Philips Systems The QC protocol will change to: QC Phantom Sagittal 3D Accelerated MPRAGE, QC Phantom Coronal 3D Non - accelerated MPRAGE and QC Phantom Axial Resting State fMRI.*



Sagittal (Example)



Coronal (Example)

Data Transfer:

Please upload all the sequences acquired for the phantom scan to the CNDA as detailed in Appendix 5.

Phantom Naming:

1. If this is the first time the phantom has been scanned, you will need to create a phantom subject in the CNDA. Please see Appendix 5 for instructions on creating phantom subjects.
2. DIAN Phantom Naming Convention (*entered during CNDA upload*):
For the upload to the CNDA, phantom scans should follow the naming convention:

Subject ID: DIAN_XXX_P_YYYY
X=Site#/P=Phantom/Y=Phantom#

For example, each phantom scan subject from site 999 should be coded:
DIAN_999_P_1234

Session ID: DIAN_XXX_P_YYYY_DDDDDD
X=Site#/P=Phantom/Y=Phantom# _DATE

For example, each phantom scan from site 999 should be coded:
DIAN_999_P_1234_080218

3. De-identification

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

Phantom Scan Results:

Mayo QC will examine the phantom data and determine if the correct parameters have been employed and assure there are no other underlying problems with the scanning session. Your site will be notified by email if the results are other than expected.

Human Volunteer Scan Instructions

1. ***After*** your site has received institutional IRB approval for the DIAN protocol and your site has passed the phantom scan qualification, one human volunteer must be scanned using the DIAN scanning protocol.
2. The volunteer should be consented by the study coordinator.
3. Since the data will be de-identified during the upload process to CNDA, please enter the volunteer's information into the scanner following standard local practice.
4. Please scan the volunteer using the instructions outlined in "MRI Subject Pre-Scan Procedures" addressed on page 9 of this manual. It is crucial to follow the appropriate pre-scan procedures, subject positioning guidelines, and DIAN sequences.

Data Transfer:

Please upload all the sequences acquired for the volunteer scan to the CNDA as detailed in Appendix 5.

Volunteer Naming:

1. If this is the first time the volunteer has been scanned, you will need to create a volunteer subject in the CNDA. This is different than obtaining an ID from DIAN Online. Please see Appendix 5 for creating volunteer subjects.
2. DIAN Volunteer Naming Convention: (*entered during CNDA upload*):
Volunteer scans should follow the naming convention:
Subject ID: XXX_V_YYYY (X=Site#/V=Volunteer/Y=Volunteer #)

For example, each volunteer scan from site 999 should be coded:
DIAN_999_V_0001

Session ID: XXX_V_YYYY_Date (X=Site#/V=Volunteer#/Y=Volunteer#/ _Date)

For example, each volunteer scan from site 999 should be coded:
DIAN_999_V_0001_080218

3. De-identification

As part of the upload process to the CNDA, all the information entered into the scanner will be removed and replaced with the information entered during the DIAN upload procedure. For this reason, you are encouraged to enter the volunteer scan information into the scanner following

standard local practice.

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. After successful qualification scanning, an official Site Qualification e-mail will be sent to the selected contacts for your site notifying them your site has been approved and is ready to scan subjects.

Volunteer Scan Protocol: *(no adjustments should be made to this protocol - Scan all as "straight" - non oblique)*

- 1) 3-Plane Localizer
- 2) Sagittal 3D Accelerated MPRAGE
- 3) Sagittal 3D Accelerated MPRAGE REPEAT
- 4) Axial T2 FLAIR
- 5) Axial Resting State fMRI - ***(Subject should have eyes OPEN)***
- 6) Axial SWI or T2* Axial GRE
- 7) DIAN Suggested DTI

Please make sure to use stereotactic marker on subjects' right temple. Please see "MRI Subject Pre-Scan Procedures" for complete instructions on scanning set-up and acquisition.

Anticipation of Hardware Upgrades:

To avoid any delays or mistakes in scanning, the Mayo QC team requires notification at least 2 weeks **PRIOR** to any software and/or hardware upgrades for any scanner involved in the DIAN imaging study so they can provide your site the correct upgraded protocols.

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

MRI Subject Pre-Scan Procedures

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 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 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.

Research Subject Naming:

Research subject ids will be generated by the Alzheimer's Disease Cooperative Study and assigned by the Clinical Study Coordinator at the clinical site prior to the MRI visit. These IDs will be seven digit numbers (e.g. 9000001). Session identifiers, which distinguish between a subject's visits, will be provided by the CNDA. These IDs will be a composite of the subjects ID, the visit number (e.g. v00, v01, v02), and the acquisition type (e.g. 9000001_v00_mr, 9000001_v01_mr).

Subject Safety and Monitoring

1. All sites should follow the standard subject consent protocols as approved by your local IRB.
2. Explain the scan procedure to the subject so that they know what to expect during the MRI.
3. Provide the subject with the opportunity to use the restroom before the scan begins.
4. 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).
5. Offer the subject hearing protection.
6. Please use standard local practice for monitoring the subject during the scan. These may include devices to monitor pulse and O₂ levels.

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).**
 - 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.**
- 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.



NOTE:

- It is extremely important that the subject is positioned in the same manner, at the nasion, for the Baseline 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.

MRI Subject Scan Protocol

MRI Scan Metadata Form

1. The “MRI Scan Metadata Form” should be completed at the time of acquisition for every DIAN subject. A copy of the MRI metadata form 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. This enables the central DIAN MRI lab at Mayo to more

closely follow each scanning session. 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 Central Neuroimaging Data Archive (CNDA) (not into DIAN Online) and this will be linked with the subjects' MRI data. Please keep a copy on site for your records.

To report an incident regarding the MRI sequences please email: DIAN-MRI@dian-info.org

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

DIAN Subject Scanning Session Includes: ALL SCANS SHOULD BE STRAIGHT-NON OBLIQUE

- 1) 3-Plane Localizer
- 2) Sagittal 3D Accelerated MPRAGE
- 3) Sagittal 3D Accelerated MPRAGE REPEAT
- 4) Axial T2 FLAIR
- 5) Axial Resting State fMRI - (*Subject should have eyes OPEN*)
- 6) Axial SWI or T2* Axial GRE
- 7) DIAN Suggested DTI

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

Entering Subject Information

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 the CNDA, the scan header will be de-identified and rendered HIPAA compliant. Data will be identified at the DIAN site by subject code only. The subject code will be in the CNDA at the time of data transmission to the CNDA. If you do not see your subject's ID, please contact cnda-help@dian-info.org.

Scan #1: 3 Plane/Tri-Planar Scout:

Example:



1. A quick acquisition in 3 orthogonal planes for anatomical orientation. One slice 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 straight, not in an oblique orientation.
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.



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.

****Pre-scan Adjustments**

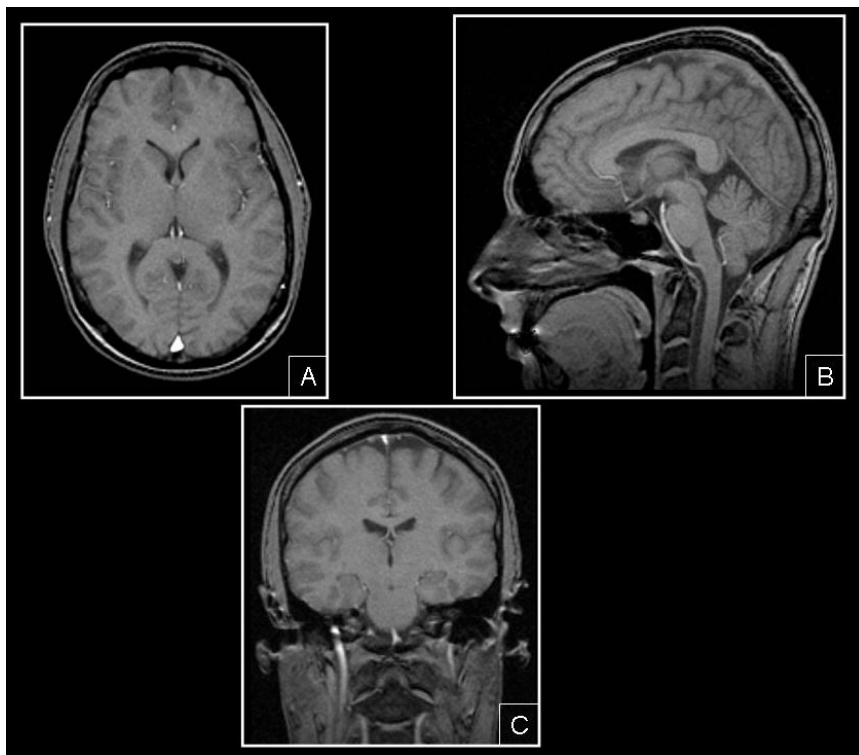
Most modern MRI scanners provide automated adjustment procedures for RF coil tuning and frequency adjustments after the subject is positioned in the magnet. Follow the adjustment procedures provided by the manufacturers.

Scan #2: Sagittal 3D Accelerated MPRAGE

Example:



1. Orientation. **Straight** sagittal. Slices will be prescribed from left to right. **DO NOT** oblique the scanning FOV to compensate for subject head 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 the nose should also be included otherwise image folding into the back of the brain will result and the exam may not be usable for the study.** Please see the images below and use as a guide to correctly position the acquisition box.



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.

Example of 3 Plane Localizer for MP-RAGE FOV Placements

Scan#3: Sagittal 3D Accelerated MPRAGE REPEAT

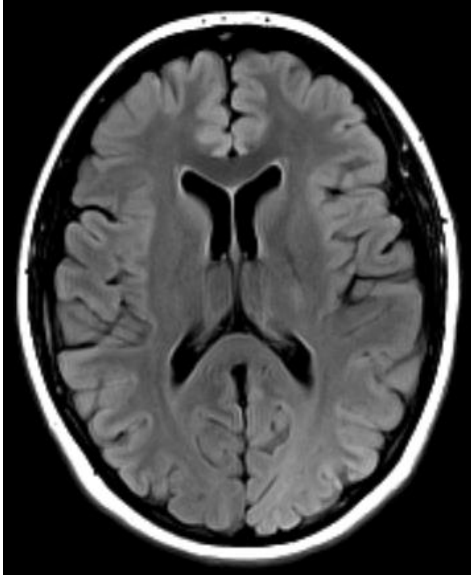
For every DIAN exam, the sagittal MP-RAGE sequence is acquired a second time, immediately after the first. Unless indicated, the scan prescription should be identical for each MP-RAGE.

The MP-RAGE is run twice for several reasons. Often subjects move to varying degrees during MRI acquisitions, so that either the first or second MP-RAGE acquisition will be of superior quality. Thus, acquiring two MP-RAGES will maximize the chance that at least one will be successful and usable for analysis. Also, in some cases, where both MP-RAGES are of good quality, it would be possible to retrospectively average the two data sets to improve the signal-to-noise. Finally, DIAN will explore the value of using the two MPRAGE scans in each exam as quasi independent data points.

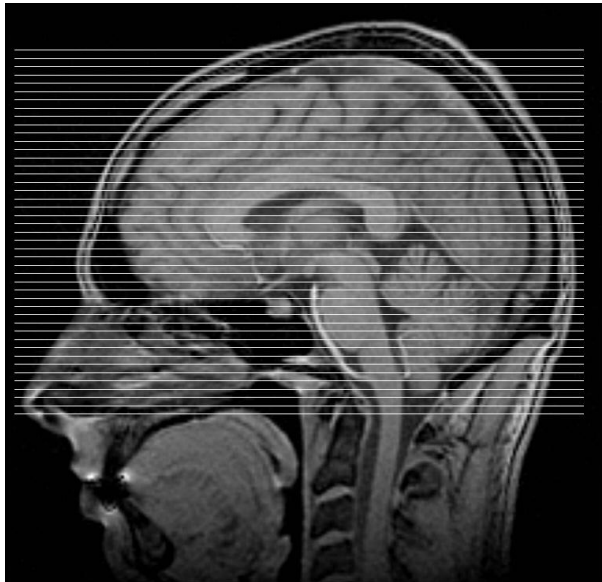
Since there are two MP-RAGES built into the DIAN scanning session, it is acceptable if one the MP-RAGES is not considered of satisfactory quality. However, if neither of the MP-RAGES is considered acceptable, you are encouraged to attempt one more additional MP-RAGE. If after three attempts, and no acceptable MP-RAGES have been acquired, please discontinue the exam and notify the study coordinator.

Scan #4: Axial T2 FLAIR

Example:



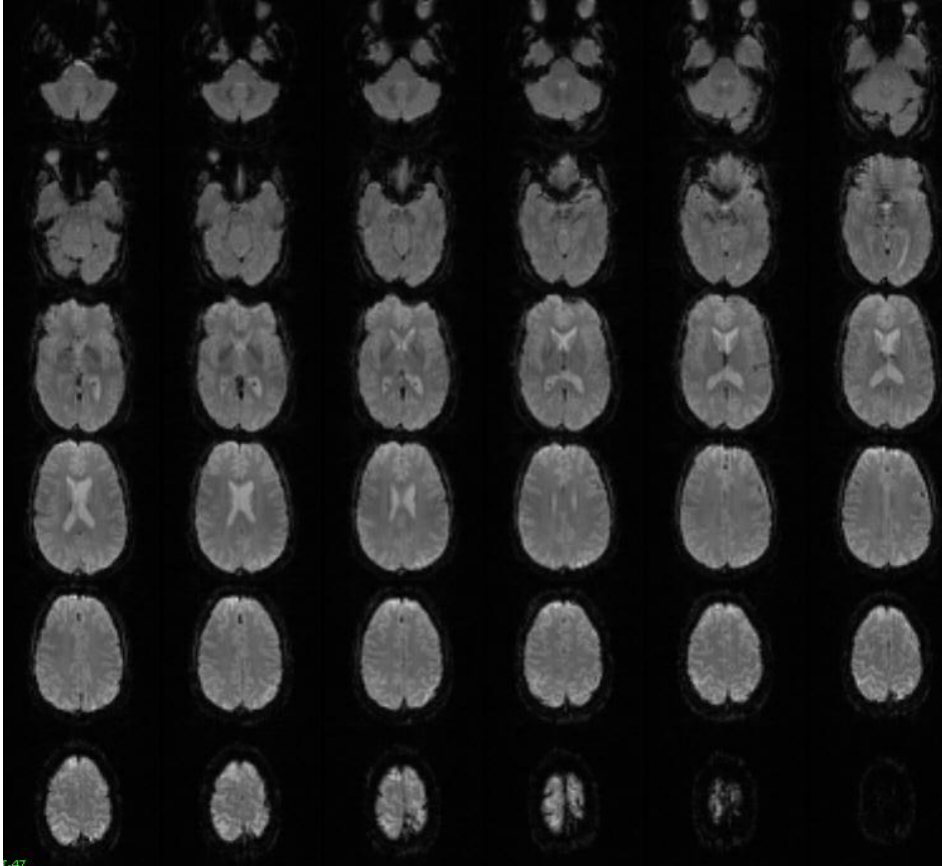
1. Orientation: **Straight** Axial. Prescribe slices inferior to superior. DO NOT Oblique Scans.
2. Positioning: Position on mid-sagittal slice from tri-planar scout. Make sure to get full BRAIN coverage. The acquisition stack should be placed just above the most superior point in the brain and should 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 head tilt. Scan as straight Axials.

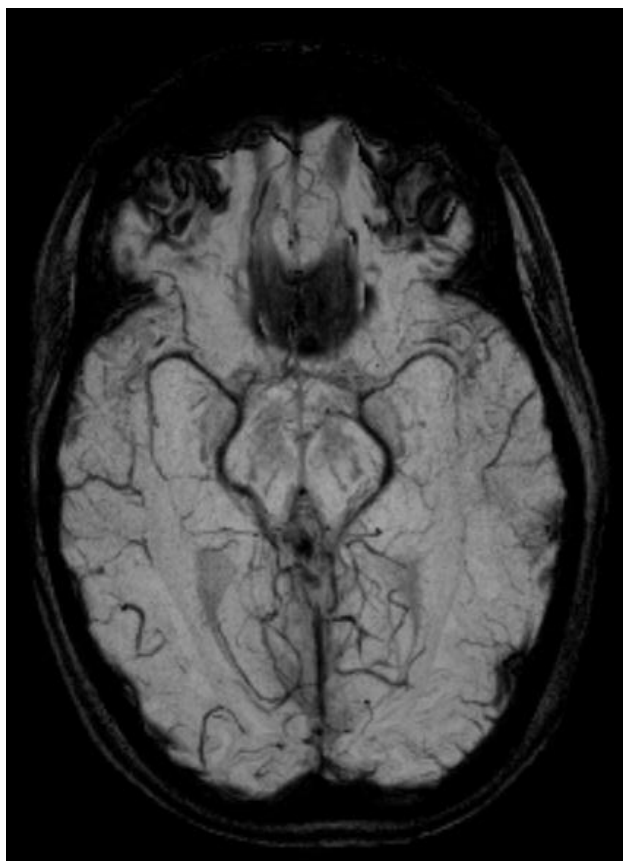
Scan #5: Axial Resting State fMRI (*Subject should have eyes OPEN*)

Example:

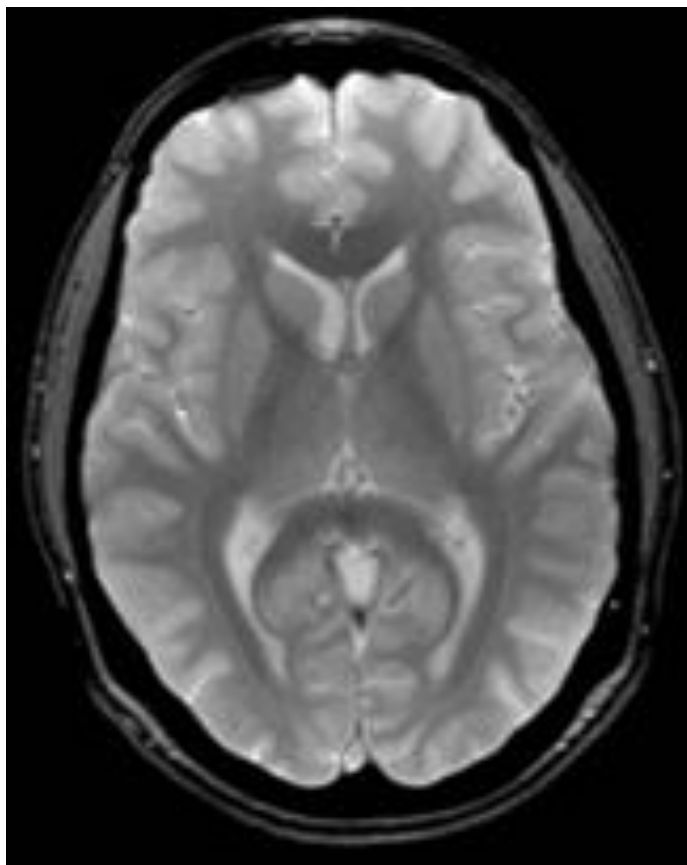


1. Orientation: Straight Axial DO NOT Oblique Scans.
2. Subject Instruction: Please instruct the subject to keep their eyes open during the entire scan. You can instruct them to focus on a point on the mirror or scanner. Also remind the subjects of the importance of holding their head still for the entire 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.***

Scan #6: Axial SWI or T2* Axial GRE (dependent on Manufacturer and/or License agreement)



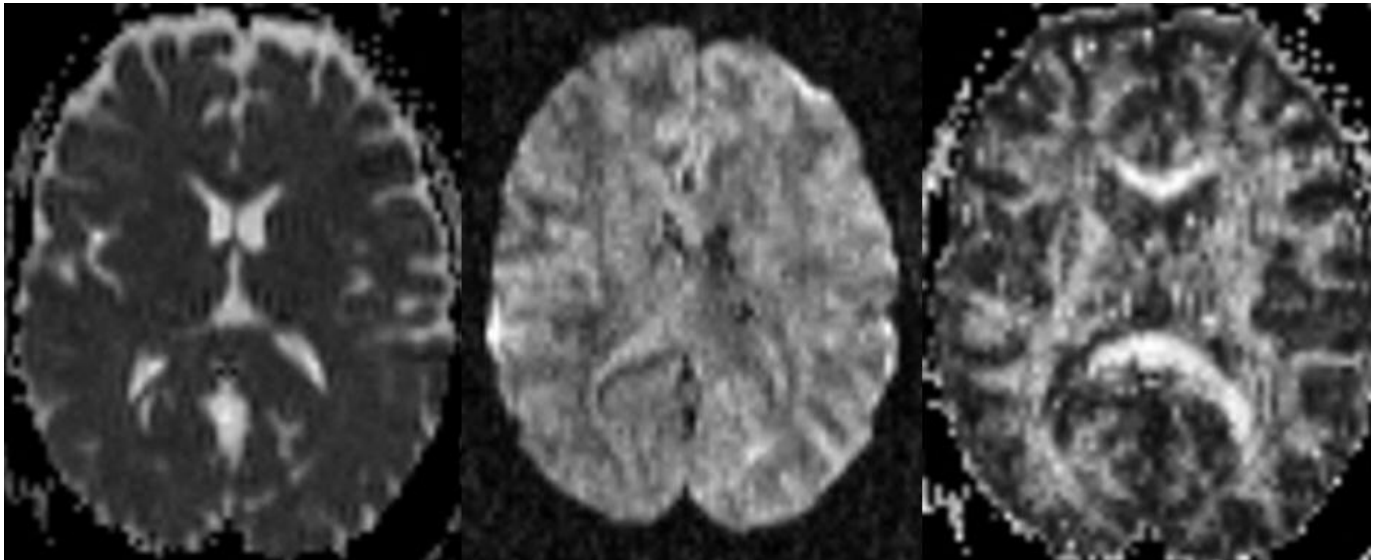
SWI



GRE

1. Orientation: Straight Axial DO NOT Oblique Scans.
2. Positioning: Position on mid-sagittal slice from tri-planar scout. Make sure to get full BRAIN coverage. 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.

Scan # 7: DIAN Suggested DTI



DTI Raw Images

1. Orientation: Straight Axial DO NOT Oblique Scans.
2. Positioning: Position on mid-sagittal slice from tri-planar scout. Make sure to get full BRAIN coverage. 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.

More information and imaging updates can be found at: http://nrg.wikispaces.com/DIAN+MRI_Updates

NOTE: The Mayo QC Team will be supplying electronic protocols (WIPs) for installation by your local service engineer for your specific MRI system(s). This will ensure that you have the correct protocol for your MRI scanner.

If you have question regarding this procedure, please contact:

DIAN-MRI@dian-info.org

Use only the imported DIAN sequences.

MRI Subject Scan Procedures

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 DIAN MRI Scan Information Sheet. The comments sections should include the reason the subject was unable to complete the MRI.

Archive Procedures

1. Every MRI for the DIAN must be archived at the MRI facility following standard local practice in addition to the data transfer to the CNDA within 24 hours of 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

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/incorrect MRI acquisition. Your site will be asked to schedule a repeat study. This is not to be confused with the repeat MP-RAGE which is part of the standard DIAN MRI protocol.
 - b. Mayo QC will check all DIAN scans to be sure that the exam was conducted on the one scanner qualified for DIAN at your site was used, and that the correct, electronically loaded sequences have been used to scan each subject. Repeat exams may also be required if the incorrect scan sequence, orientation, or angulations are used. It is imperative to use the DIAN approved acquisition sequence with every DIAN subject. Scans with image degradation due to the incorrect scan sequence, orientation, or angulations will **NOT** be reimbursed nor will scans acquired on any scanner other than the one qualified for DIAN. 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 Mayo QC team 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.

On-Going Quality Control and Post-Subject Phantom Scanning

To ensure scanner stability and scan quality throughout the DIAN study, each site is **required** to perform **BI-MONTHLY** quality control scans on the DIAN phantom using the DIAN QC Phantoms protocol. These scans should be completed on the first business day of every other month. Bi-Monthly reminders will be sent out approximately one week prior to the month a scan is due.

Bi- Monthly Quality Control (QC) Phantom Scanning Instructions

For the on-going quality control and post processing image analysis, each site must scan the specially designed DIAN phantom using the electronically loaded DIAN QC protocols on a bi-monthly basis.

Bi-Monthly QC Phantom Scan Protocol:

- 1) Localizer
- 2) QC Phantom Sagittal 3D Accelerated MPRAGE
- 3) QC Phantom Sagittal 3D non-accelerated MPRAGE
- 4) QC Phantom Coronal 3D non-accelerated MPRAGE

****(For Siemens Systems VB17 and Current Release Philips Systems The QC protocol will change to: QC Phantom Sagittal 3D Accelerated MPRAGE, QC Phantom Coronal 3D Non - accelerated MPRAGE and QC Phantom Axial Resting State fMRI.*

The on-going quality control phantom MP-RAGE scans are nearly identical to the subject MP-RAGE scans except for the slice thickness has been increased to ensure that the phantom has been covered completely. In addition, 2 of the three are not accelerated – plus one is in the coronal plane.

IMPORTANT:

If a site fails to perform these phantom scans and/or they have not been performed within 2 weeks of the due date, DIAN will not accept or reimburse the subsequent subject scans. The study coordinator and the principal investigator at each site will be notified if a phantom scan has not been received within that time frame.

NOTE: The Mayo QC Team will be supplying electronic protocols (WIPs) for installation by your local service engineer for your specific MRI system(s). This will ensure that you have the correct protocol for your MRI scanner.

If you have question regarding this procedure, please contact:

DIAN-MRI@dian-info.org

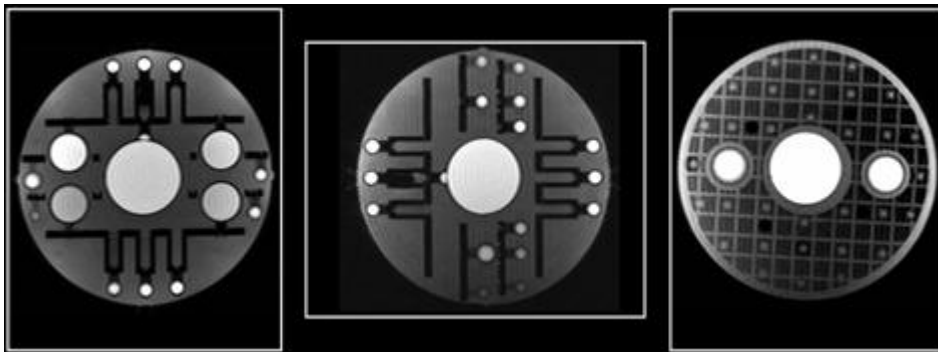
Phantom Positioning:

The following image shows the phantom placed in the appropriate position within the 8-channel coil. Achieving a reproducible position is a key element to the system performance analysis that will be

conducted after each DIAN subject that is imaged. We hope that positioning with the alignment lines upward and the serial number SN XXXX positioned out of the bore as shown, will facilitate the reproducible positioning of your phantom.



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



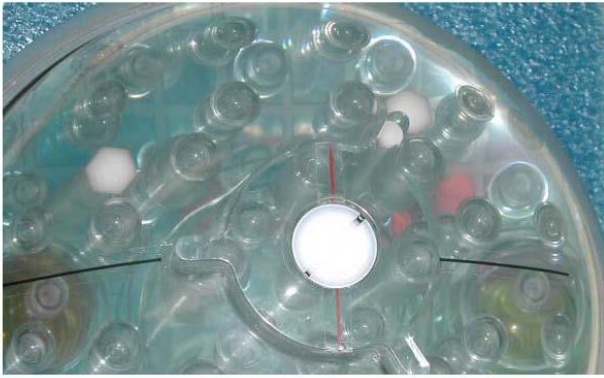
Please note that your phantom has a base and positioning markers (in black and red, see image below). The phantom should be placed inside the head coil with the alignment markers facing upwards. This orientation is due to space constraints within some coils and we would like to maintain a consistent orientation for all scanners across the DIAN study.

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 markers up, and the phantom SN number (e.g. 9999) 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 Naming:

1. If this is the first time the phantom has been scanned, you will need to create a phantom subject in the CNDA. Please see Appendix 5 for instructions on creating phantom subjects.
2. DIAN Phantom Naming Convention (*entered during CNDA upload*):
For the upload to the CNDA, phantom scans should follow the naming convention:

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

For example, each phantom scan from site 999 should be coded:

DIAN_999_P_9999_080218

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

Data Transfer:

Each site will send the phantom data to the CNDA within 24 hours after the completion of the scan as detailed in Appendix _5.

Measurements:

The Mayo QC team will perform the following measurements on the phantom data: linear scaling, Gradient non-Linearity Measurements, and Signal to Noise measurements.

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.



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

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.

DIAN

MRI Screening Tool

-THE FOLLOWING ITEMS MAY BE PERSONALLY HARMFUL AND OR INTERFERE WITH MRI SCAN.

-A **YES** or **NO** answer must be provided for every item. If any question, please ask a staff member for help.

YES NO

- Are you Claustrophobic?
- Cardiac pacemaker/pacer wires/ or defibrillator?
- Any Coil, filter, stent or valve (Type_____)
- Aneurysm clip(s)
- Implanted drug pump(s) (Type_____)
- Penile Implant (Type_____)
- Tissue Expander (e.g. breast)
- IUD or Pessary (Type_____)
- Orthopedic fixation device, internal or external?
- Any implanted items (e.g. pins, rods, screws, wires, nails or plates)
- Artificial limb or joint. Location:_____.
- Any type of metal objects, shrapnel or bullet anywhere on your body?
- Cochlear implant or Stapes Implant?
- Hearing aid(s) (**Remove before MRI Scan**)
- Eyelid spring/artificial eye?
- Medication patch (Hormone patches, nicotine, catapres-TTS)
(**Remove before MRI Scan**)
- Shunt?
- Allergies:_____
- Implanted Radiation seeds for cancer treatment?
- Removable dentures, false teeth or partial plate?
- Tattoos or tattooed eyeliner?
- Any history of Cancer?
- History of Chronic Renal disease?
- Receiving Hemodialysis/Peritoneal Dialysis?
- Renal Transplant or evaluation for Renal Transplant?
- List surgical procedures/operations: _____
- Braces
- Do you have any metallic foreign objects in your eyes?

Please remove following:

**Keys
Hairpins
Barrettes
Jewelry
Watch
Safety Pins
Credit Cards
Money Clips
Coins
Pens
Belt
Metal Buttons
Pocket Knife
Beeper
Cell Phone
Clothing with Metal**

YOU MAY BE REQUIRED TO WEAR EARPLUGS OR EARPHONES DURING THE SCAN:

I attest that the above information is correct to the best of my knowledge. I have read and understand the entire contents of this form and I have had the opportunity to ask questions regarding the information on this form.

Print Participants Name: _____

Participants Signature: _____ **Date:** _____.

Signature of Person completing form _____.

Appendix 2: MRI Scan Information Sheet

The “MRI Scan Information Sheet” should be completed at the time of acquisition for every DIAN 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.

Documentation -- MRI Scan Metadata Form

IMPORTANT: You must use the electronically provided DIAN protocols on your DIAN qualified scanner.

*Be sure to complete the MRI scan metadata form fully *as the study is being acquired*.

*The MRI scan information sheet must be provided back to the study coordinator following the scan.

Appendix 2--Sample MRI Scan Metadata Form

DIAN - MRI - Scan Information

3T Scan Information

Participant:

		/ /
Participant ID	Session ID	Date of Scan

Visit: Initial; Follow-up__

Site Code:

Study Coordinator Name:

DIAN Participant Initials:

MRI Technologist Initials:

****Important:** It is mandatory that the DIAN site qualified scanner be used for ALL participants in the DIAN study. ****It is also mandatory that the same DIAN approved sequences are used for all DIAN subject scans. Do NOT adjust protocol values.**

Was the scan conducted?

- Yes
 No

Reason why the scan was not conducted:

- Illness
 Participant unavailable
 Participant unwilling
 Administrative problems
 Withdrawn consent
 Other (specify)

If Other, specify:

Placed Marker on the subjects Right (RT) temple.

Yes No

****Dependent on your software revision the order of scans may be different than stated.****

Scan #1: 3 Plane/Tri-Planar Scout: **Check the subject positioning in the head coil; Re-position and re-scout if necessary.

Completed?

Yes

No

NOTES:

Scan #2: Sagittal 3D Accelerated MPRAGE: ** Straight sagittal. **DO NOT** oblique the scanning FOV to compensate for subject held tilt. Position FOV to avoid nose wrapping into the back of the brain.

Completed?

Yes

No

NOTES:

Scan #3: Sagittal 3D Accelerated MPRAGE REPEAT: Should be an exact duplicate of scan #2 unless repositioning is necessary

Completed?

Yes

No

NOTES:

Scan #4: Axial T2 FLAIR: Position Slices to cover below cerebellum through the top of the head. **DO NOT** oblique the scanning slices.

Completed?

Yes

No

NOTES:

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

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 subject prior to this scan that they should have their eyes open and to hold very still. **DO NOT oblique the scanning slices.

Was the subject instructed to open their eyes?

- Yes
- No

Completed?

- Yes
- No

NOTES:

Scan #6: Axial SWI or T2* Axial GRE (dependent on Manufacturer and/or License agreement):

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

Completed?

- Yes
- No

NOTES:

Scan #7: DIAN Suggested DTI

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

Completed?

- Yes
- No

NOTES:

Patient Motion Problems:

- Yes
- No

If yes, describe:

Scanner malfunction:

- Yes
- No

If yes, describe:

Other protocol variations:

Yes

No

If yes, describe:

Was data transferred to CNDA within 24 hours of scan?

Yes

No

Data must be transmitted to CNDA within 24 hours of the MRI scan. If your site is unable to complete the transfer within 24 hours please indicate the problem in the "Comments" section below.

Transfer Date:

Month/Day/Year

Comments

Data Archived Locally

If No, please explain under comments.

Yes

No

Archive Medium (circle): PACS CD/DVD MOD

Other:

Comments :

Appendix 3: MRI Acquisition Summary

- 1) 3-Plane Localizer
- 2) Sagittal 3D Accelerated MPRAGE
- 3) Sagittal 3D Accelerated MPRAGE REPEAT
- 4) Axial T2 FLAIR
- 5) Axial Resting State fMRI - (*Subject should have eyes OPEN*)
- 6) Axial SWI or T2* Axial GRE
- 7) DIAN Suggested DTI

Phantom Scans:

- 1) Localizer
- 2) QC Phantom Sagittal 3D Accelerated MPRAGE
- 3) QC Phantom Sagittal 3D non-Accelerated MPRAGE
- 4) QC Phantom Coronal 3D non-Accelerated MPRAGE

****(For Siemens Systems VB17 and Current Release Philips Systems The QC protocol will change to: QC Phantom Sagittal 3D Accelerated MPRAGE, QC Phantom Coronal 3D Non - accelerated MPRAGE and QC Phantom Axial Resting State fMRI.*

NOTE: The DIAN MRI core will be supplying electronic protocols (WIPs) for installation to your local service engineer for your specific MRI system(s). This will ensure that you have the correct protocol for your MRI scanner.

If you have question regarding this procedure, please contact:

DIAN-MRI@dian-info.org

Use only the imported DIAN sequences.

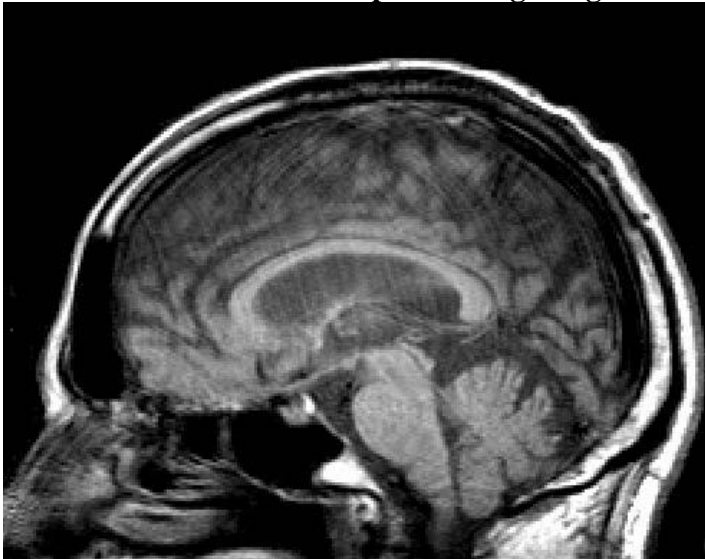
Appendix 4: DIAN Acquisition Troubleshooting Guide

Superior image quality is imperative to the success of the DIAN study. Every effort should be made to acquire excellent scans on DIAN subjects at their first MRI appointment and at all subsequent visits. This prevents the clinical centers from rescheduling additional repeat MRI's for subjects.

It should also be noted that the MPRAGE acquisition sequence is the most important sequence in the DIAN. This sequence should always be acquired immediately after the tri-planar scout. Please note the image quality of this scan and re-acquire if necessary before running the rest of the sequences (FLAIR, etc.).

Please use the following reference as a guide for identifying and remedying inferior image quality, image artifacts, and subject issues that may degrade image quality. Also, please contact DIAN-MRI@dian-info.org for specific technical questions or concerns outside the scope of this manual.

Example 1: Image Degradation due to Movement Artifact



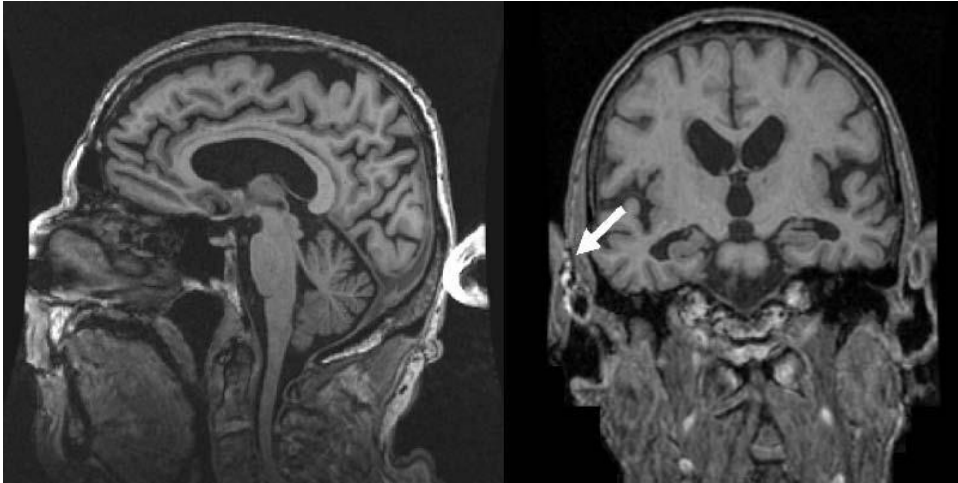
Problem:

In this example movement has caused motion artifacts. Acquisitions with major motion artifacts will not be accepted and a repeat scan may be requested.

Possible Remedies:

1. If movement is due to the subject's head moving, reacquire MPRAGE after tightly securing the subject's head with additional restraints and discussions with subject to hold their head still.
2. If the subject is not moving it is possible the artifact is the result of mechanical problems. Please discuss with your service engineer.

Example 2: Wrap Around



Problem:

In this example, wrap around occurs in the MPRAGE image above. In the figure on the left, the nose folds into the back of the skull. In the figure on the right, the ear wraps into the side of the skull. Acquisitions with wrap around artifacts will not be accepted and a repeat scan will be requested.

Possible Remedy:

1. Wrap around generally occurs when the subject's head size is larger than the acquisition box. If the acquisition box does not fully cover the subject's head (including the nose), increase the FOV and increase the number of phase encoding steps accordingly so as not to change the pixel resolution of the image.
2. Reposition the MPRAGE acquisition box to cover the entire head (including the nose) and rescan.

Example 3: Signal Loss at the Top of the Brain



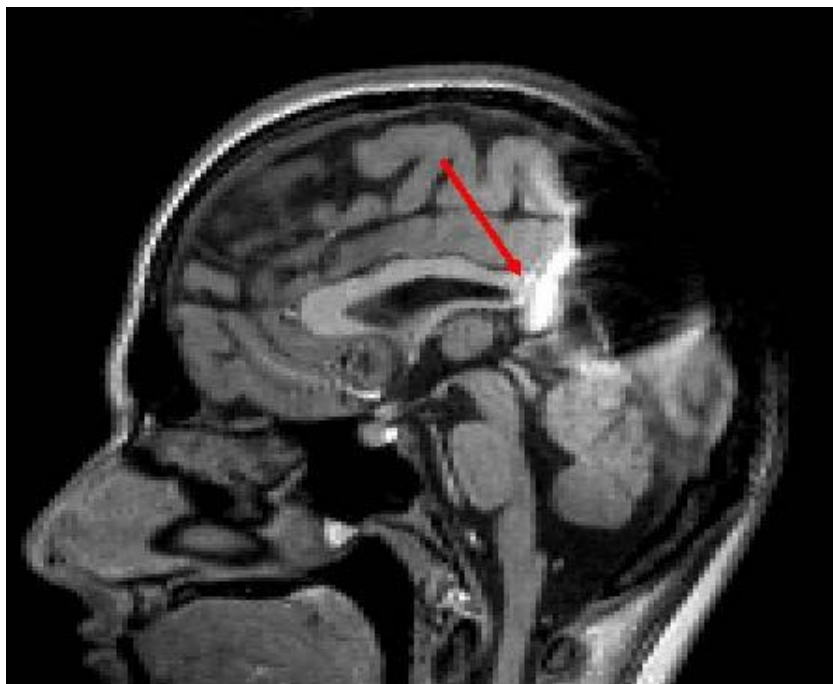
Problem:

In this example, the image has a loss of signal at the top of the brain due to incorrect positioning in the head coil. The subject was placed too high in the coil. Please note the lack of contrast between gray and white matter at the top of the brain only. Acquisitions with signal loss, especially due to incorrect positioning, will not be accepted and a repeat scan will be requested.

Possible Remedies:

1. Check to be sure subject is positioned correctly in the head coil. Please see “Subject Positioning” for information on positioning.
2. Make sure head coil is properly secured.

Example 4: Metal Artifact



Problem:

Magnetic field distortions: In this example there is a signal void due to the presence of metal near the subject's head. Acquisitions with metal artifact will not be accepted any circumstances and a repeat scan will be requested.

Possible Remedy:

1. Make sure the subject is not wearing any metal. Refer to Appendix 1. Check for hair clips, metallic makeup (i.e. permanent eyeliner), necklace, safety pins, removable dentures, and facial jewelry. Remove metal and rescan.