

**Quick Reference Guide for the Acquisition of Subject MRI Scans of the Brain****STUDY OVERVIEW**

- Protocol CCNP520A220J is a randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of CNP520 in participants at risk for the onset of clinical symptoms of Alzheimer’s Disease (AD).
- The purpose of the study is to determine the effects of CNP520 on cognition, global clinical status, and underlying AD pathology in people at risk for the onset of clinical symptoms of AD. The study will assess progression to clinical symptoms in participants treated with CNP520 compared to placebo.
- Subject MRI scans are required at Screening (Scr4 v104) and Weeks 26 (Y1Q2 v203), 52 (Y1Q4 v205), 104 (Y2Q4 v209), 156 (Y3Q4 v213), 208 (Y4Q4 v217), 260 (Y5Q4 v221), 312 (Y6Q4 v225), 364 (Y7Q4 v229) and end of study (EoS v301). Subject that terminate early will complete an early termination scan (visit name PPWTEC v299)
- All MRI data must be sent to Bioclinica within 1 business day of acquisition for centralized Quality Control and analysis.

ENTERING STUDY SUBJECT DATA IN THE ELECTRONIC HEADER

- In order to ensure study subject confidentiality, please enter the following information into the specified fields in the digital (DICOM) MRI header when acquiring exams:
In the **Subject Name** field, enter: **[4-digit Site ID Number] - [7-digit Subject ID Number]**
In the **Date of Birth** field, enter: **01/JAN/YYYY** (Enter the actual year of birth and use January 1st for the remainder)
In the **Study Description** field, enter: **Visit name** (Scr4 v104, Y1Q2 v203, Y1Q4 v205, Y2Q4 v209, Y3Q4 v213, Y4Q4 v217, Y5Q4 v221, Y6Q4 v225, Y7Q4 v229, EoS v301, PPWTEC v299 or Unscheduled)

IMPORTANT - Data in the digital header must match the accompanying transmittal form.

More details can be found in section 7.1 of the MRI Procedure Manual.

MRI SEQUENCE ACQUISITION – PROTOCOL CONTENT

- Sequences to be scanned in exact order:
 1. **3D T1**-weighted (Coronal IR-prepped Fast SPGR / Sagittal 3D TFE / Sagittal MPRAGE)
 2. 2D Axial **FLAIR**
 3. 2D Axial **T2*** Gradient Echo
 4. 2D Axial **PD/T2** Turbo/Fast Spin Echo
 5. 2D Axial **DWI**
All b=0 and b=1000 images must be provided, as well as ADC maps.
 6. 2D Axial **DTI**
All b=0 and b=1000 images must be provided.
 7. 2D Axial Phase and Magnitude **GRE Field Mapping**
 8. 2D Axial Resting State **BOLD fMRI**
 9. Repeat **3D T1**-weighted (identical parameters as in #1)
- If a phased-array coil is used, please use PURE (GE), CLEAR (Philips) or Prescan Normalize (Siemens) to reduce RF inhomogeneities. For older GE scanners, do not use SCIC instead of PURE.
- If the patient’s head is too large to fit the available phased-array coil, it is permissible to use a birdcage coil instead.
- If you start the study with a regular head coil, you may not switch to a phased-array coil during the study. Further, if you start with a particular multi-channel phased array coil, you may not switch coils during the study, even if the imaging facility acquires an RF coil with more elements.
- Please refer to the system-specific table annexed to this document for details regarding MRI parameters. The first page contains parameters for the above sequences. The second page is for phantom scans only.

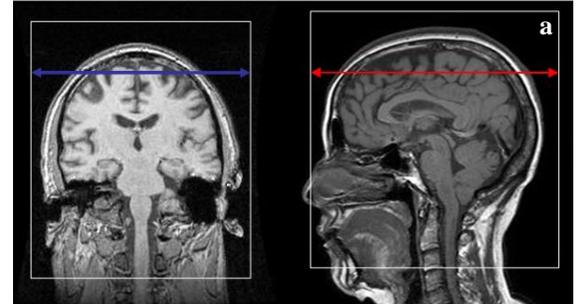
More details can be found in section 7.2 of the MRI Procedure Manual.



MRI SEQUENCE ACQUISITION - POSITIONING AND ANGULATION

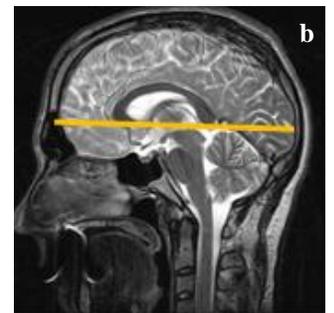
3DT1

- Used to provide information on brain structure and perform volumetric measurements.
- Orientation must be Coronal for GE scanners, and Sagittal otherwise (Philips, Siemens).
- Position the volume as shown in fig. a. The **Blue** and **Red** lines show the slice and phase directions, depending on your scanner.
- Be sure to cover the brain both LR and AP. Leave about 15 mm from top of the head to the top of the FOV.



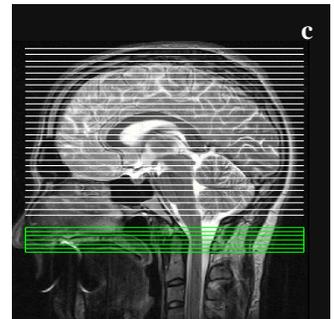
Axial FLAIR

- Used to detect ARIA-E, white matter lesions, lacunes and infarcts.
- Position and angulate on sagittal localizer that shows best image of anterior commissure and posterior commissure (AC-PC).
- Angulate parallel to AC-PC line (see **orange** line on fig. b).
- Acquisition stack must fully cover subject's brain, starting at the vertex down to the cerebellum (see white stack on fig. c).



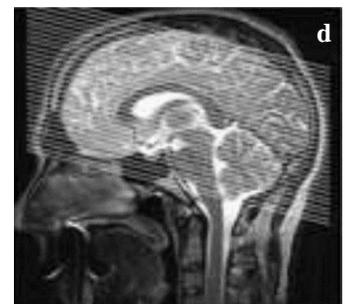
Axial T2* GRE, Dual Echo PD/T2 and DWI/DTI

- T2* is used to detect ARIA-H, PD/T2 in conjunction with FLAIR for white matter disease and DWI/DTI for acute stroke.
- Copy positioning and angulation from Axial FLAIR for prescription of T2*.
- Use similar angulation for PD/T2, with a 50-mm flow saturation band inferior to the MRI slices and positioned about 15-mm from the bottom of the MRI stack to reduce inflow effects (see green lines on fig. c).
- Use orthogonal axial orientation for DWI and DTI. Please submit Trace and ADC maps along with all native images (b=0 and b=1000).



GRE Field Mapping and Axial BOLD fMRI

- Used to assess inherent functional connectivity within resting state networks.
- Angulate parallel to AC-PC line, then tilt 15 degrees toward TOP of head (see fig. d).
- Field Mapping and fMRI must have identical slab orientation and position. Copy slab from Field Mapping to fMRI.
- Instruct subject to **KEEP EYES OPEN AND STAY AWAKE** for duration of scan (10 minutes).



More details can be found in section 6.2 of the MRI Procedure Manual.

For any question regarding MRI acquisition, please contact NVS-CNP520@bioclinica.com

**MRI SEQUENCE ACQUISITION – GENERAL STUDY GUIDANCE**

- **Consistent image acquisition** throughout this clinical trial is of utmost importance!
- For each follow-up visit, retrieve and use a subject's screening exam to ensure the settings and parameters are consistent between visits.
- The protocols below should be stored in your scanner and used for all visits
- The order of acquisitions should correspond to that indicated on the previous page.
- Instruct the subject about the importance to **avoid any head motion** for the entire MRI exam. Record any subject difficulties on the transmittal form.
- All MRI data must be sent to Bioclinica within 1 business day of acquisition for centralized Quality Control and analysis.

For any question regarding MRI acquisition, please contact NVS-CNP520@bioclinica.com

ELECTRONIC DATA SUBMISSION

- Bioclinica provides a secure website to submit data for those facilities that can upload MRI images via the Internet at the following address: <https://smart.bioclinica.com>
- Bioclinica will provide a personal login and password for each MRI technologist participating in the study.
- To transmit images using the SMART Portal (formerly known as SynarcConnect), please follow the below steps:
 1. Navigate to <https://smart.bioclinica.com> and enter the Username and Password provided by Bioclinica.
 2. You will be directed by default to the **File Upload Activities Summary** page.
 3. Click on the **“Upload Files”** button, and you will be brought to the **Transmittal Form** page.
 4. Select the Phantom or Subject Transmittal Form, depending on the content of your upload.
 5. Enter the required information (see first page of this document) and click on the **“Submit and Upload”** button.
 6. On the **File Uploads** page, click on **“Add Folders/Files”** to select files from your local system.
 7. Once all the files are added, click on the **“Upload Files”** button.
 8. Once upload status is **“Upload Complete”**, enter your password again to **“Sign and Complete”** the upload.
 9. You will be directed to the **Upload Confirmation** page. A confirmation email will be sent to you as a receipt. **Please note**, if you do not receive this email, the image files were not successfully uploaded to Bioclinica.

More details can be found in section 9.0 of the MRI Procedure Manual.

For any question or issue regarding data transfer, please contact helpdesk@bioclinica.com