Use of ADNI MRI Methods for Non-ADNI Studies **Version 1: 6-26-2006**

ADNI has received a number of inquiries about making ADNI methods available for non-ADNI studies. For MRI, this topic can be divided into three areas, which are addressed individually below. These are the imaging protocol, image corrections, and the ADNI phantom and analysis software.

IMAGING PROTOCOL

The ADNI Exam consists of the following sequences:

Subject Scan

1. Localizer/Scout Scan (20 secs)
2. Straight Sagittal 3D MPRAGE (7-10 mins)
3. Straight Sagittal 3D MPRAGE - REPEAT - (7-10 mins)
4. B1 Calibration Scan Phase Array Coil *(if applicable)* (30 secs)
5. B1 Calibration Scan Body Coil *(if applicable)* (30 secs)
6. Axial Dual Echo T2 FSE (5-7 mins)

ADNI Phantom - Quality Control Scans (following subject scan)

1. Localizer/Scout Scan (20 secs)
2. Straight Sagittal 3D MPRAGE (8-10 mins)

Total Scan Time with Phantom 40-45 mins

The ADNI MRI core has worked closely with contacts at General Electric Healthcare, Siemens Medical Solution and Philips Medical Systems to create protocols which, for a given field strength, produce very similar spatial resolution, contrast, and SNR properties, across vendors and across various systems within each vendor product line. System-specific ADNI protocols can be found listed by MR vendor at the following link: http://www.loni.ucla.edu/ADNI/Research/Cores/. Also, a Message/Billboard has been created allowing users to post questions, comments: www.loni.ucla.edu/ADNI then select billboard.

The localizer, and axial dual echo fast spin echo (or turbo spin echo) sequences used in the ADNI protocol are product sequences for all systems; and therefore do not require installation of any special (non-product, also called works-in-progress, WIPS or research) software on the MRI system. The 3D T1-weighted sequence used for morphometric analysis in ADNI is the MPRAGE. Because the MRI portion of ADNI is primarily focused on brain morphology, the MPRAGE sequence constitutes the heart of the ADNI MRI protocol. This sequence is repeated in the protocol in order to increase the probability of obtaining at least one high quality morphometric scan in each exam, and thereby minimize the probability that the subject will need to be rescanned because of scan quality problems (e.g. motion artifact, etc). Variations among the MR manufacturers and within manufacturer product lines exist with respect to the need for image corrections. Also the availability of an MPRAGE pulse sequence that produces images acceptable for ADNI, or an MPRAGE-like equivalent imaging sequence varies across and within manufacturer product lines.

The ADNI MPRAGE sequence is equivalent to product for Siemens systems running software release VB13 and later, and for Philips systems. It is similar to product for Siemens systems before release VB13. (Also for the Siemens systems a WIPS pulse sequence was required for the B1-calibration prior to release VB13). The ADNI MPRAGE differs from the analogous product on GE systems (IR-FSPGR). Consequently, for the ADNI study, an electronic protocol (but no WIPS pulse sequence) was distributed to ADNI Philips sites. The pulse sequence(s) and electronic protocol software were distributed as a Works-In-Progress (WIP) disc for installation on Siemens and GE scanners. Therefore if you wish to incorporate the ADNI MRI methods into your study we suggest the following:

Philips Systems – use the system specific parameters outlined at: http://www.loni.ucla.edu/ADNI/Research/Cores/. Using this .PDF documentation, you can enter in the appropriate pulse sequence parameters into your system to replicate the acquisition method used for ADNI. The appropriate Philips contact for information about ADNI is Gregory Metzger PhD (gmetzger@cmrr.umn.edu).

Siemens Systems – the pulse sequence parameters at http://www.loni.ucla.edu/ADNI/Research/Cores/ will result in similar image properties when used with the product MPRAGE on pre-VB13 systems. (Note that for VB11 and VB12 systems, protocols that use the "prescan normalization" feature rather than the ADNI B1-calibration are—scheduled to be posted for non-ADNI studies in late summer 2006. This removes the need to obtain any WIPS pulse sequences.) Final crossover testing is still underway, but product MPRAGE at VB13 and beyond seems likely to be indistinguishable from the ADNI MPRAGE. However, if you wish to obtain access to the Siemens ADNI WIP (i.e., the actual ADNI pulse sequence(s) and protocol for Siemens systems), then you should contact Ravi Seethamraju PhD (ravi.seethamraju@siemens.com).

General Electric Systems– Two options exist for obtaining an ADNI or ADNI-like inversion prepared 3D T1-weighted pulse sequence.

Option 1) use the GE product IR-SPGR sequence. The GE product imaging sequence which most closely resembles the ADNI MPRAGE is IR-FSPGR. GE has added enhancements needed to create a high quality ADNI-like IR-FSPGR to software version 14.0M4, which is scheduled for release in July 2006. The product IR-FSPGR sequence on pre-14.0M4 systems is incompatible with the ADNI protocol in several important ways. For this reason we do not recommend option 1 for employing pre-14.0M4 systems in studies attempting to incorporate ADNI-like MRI methods. IR-FSPGR parameters needed to reproduce an ADNI-like inversion prepared 3D T1-weighted sequence with 14.0M4 will soon be available at http://www.loni.ucla.edu/ADNI/Research/Cores/.

Option 2) obtain the ADNI MPRAGE sequence on CD. This is a viable option for 1.5T systems running software levels 9.1, 11.0M4, 12.0M3A, 12.0M4, 14.0M3 and above. For studies interested in including 3T systems, the ADNI MPRAGE pulse sequence is available for software release VH3 M4, G3, E2, 12.0M4, and 14.0M3 and higher, as well. Matt Bernstein PhD at Mayo Clinic, Rochester can distribute the ADNI MPRAGE CD compiled at the appropriate system level directly to study sites – but only when all of the following important provisions can be met: First, the MRI system must be run in research mode. Therefore, unless the MRI system already has research mode enabled, the site will need to work with Sandhya Parameswaran PhD at GE to complete a re-

search key agreement with GE. Second, the study will have to pay for expenses incurred by Matt Bernstein and Bret Borowski for providing support such as creating and sending the CD, answering support question by email, and associated paperwork. Third, the study will need to obtain prior permission from the University of Virginia (UVA) Intellectual Property Office for permission to use of MPRAGE for the study. This is because University of Virginia holds the MPRAGE patent. (Matt Bernstein can provide contact information for how to get that permission from UVA.) Finally, each of the GE sites participating in the study will have to sign off on GE's standard site-to-site pulse sequence sharing letter agreement with Mayo. This site to site agreement must be signed as is, with no attempted one-of-a-kind modifications by individual sites. Contact information for option 2 is: Matt Bernstein PhD (mbernstein@mayo.edu), Sandhya Parameswaran PhD (sandhya.parameswaran@med.ge.com).

IMAGE CORRECTIONS

In the actual ADNI study, three types of image non-ideality are corrected by ADNI after the images have been acquired. These are geometric distortion due to gradient nonlinearity, image intensity non-uniformity due to the non-homogeneous characteristics of some RF receiver coil designs, and image non-uniformity due to wave effects (i.e., the so-called “dielectric resonance”) at 3T. These three effects are addressed individually.

Gradient nonlinearity: On some MR systems linearity has been traded off for improved gradient performance characteristics. Gradient nonlinearity results in spatial distortion which should be corrected in all three spatial dimensions for high quality morphometric analyses.

Philips systems: The native images acquired without correction are sufficiently linear for the purposes of ADNI, so no non-linearity correction is employed in ADNI.

Siemens systems: 2D in plane distortion correction is offered as product (although not as the default operating mode) on systems operating at level VB11 and higher. 3D nonlinearity correction is available on Siemens systems at VB13 as a purchasable option.

GE systems: 2D in-plane distortion correction is the default operating mode of all current GE systems. 3D nonlinearity correction (i.e., correction in the slice direction as well) is currently not available as a product feature.

BRM gradient systems seem to require only minimal correction for nonlinearity. Although ADNI does incorporate 3D correction for images acquired on BRM systems, this might not be absolutely necessary, depending on the specific aims of the study. GE systems with TRM (i.e., TwinSpeed) gradients (operating in zoom mode as in the ADNI protocol) will require this correction in 3D.
Because correction for gradient nonlinearity contains proprietary information about gradient coil design, the correction methods cannot be distributed publicly. One option for obtaining 3D correction for gradient non-linearity of MPRAGE images acquired on GE or Siemens systems is to have Anders Dale PhD (amdale@ucsd.edu) process the images in his laboratory.

Intensity non-uniformity due to non-homogeneous RF receiver coil profiles: For the ADNI imaging protocol, this non-uniformity generally presents itself as a dark center and bright periphery pattern on receive coils—especially multi-element phased arrays (also known as "matrix coils", etc). Correction for this non-uniformity is available from the manufacturers. On Philips system the correction is called CLEAR, on GE systems PURE, and on Siemens systems PRESCAN NORMALIZE. CLEAR is present on all Philips systems that support multi array receiver coils. PURE is present on 1.5T GE systems at version 12.0 and beyond but is not yet available at 3.0T. PRESCAN NORMALIZE is present on all Siemens systems at the TIM level and beyond. Data from older MRI systems may be corrected for RF receiver coil non-uniformity by contacting Anders Dale (amdale@ucsd.edu) provided the appropriate B1-correction scans are acquired. Note that on some pre-VB13 Siemens systems this might require a WIPS pulse sequence.

Intensity non-uniformity due to wave effects of 3T: The RF wavelength at 3T is half that at 1.5T. One consequence of this is an artifact known by various names, including wave effect or dielectric resonance. This presents as a bright center and dark periphery pattern in the head. At present no correction for this is offered by MR manufacturers to our knowledge. A correction for this has been incorporated in ADNI image preprocessing. When available the ADNI software application will be available under the heading "dielectric correction" at the following link http://www.loni.ucla.edu/ADNI/Research/Cores/. Note, that this application is a wrapper script written in perl and makes extensive use of publicly available packages including AIR, N3 and tools from the NIFTI initiative. ADNI MR Core makes the wrapper script and associated documentation freely available, however the ADNI MRI core cannot provide software support.

ADNI PHANTOM AND ANALYSIS SOFTWARE

Each human subject MRI scan in ADNI is accompanied by scan of a phantom for quality control purposes. The phantom and the associated analysis software are designed to measure several properties. These include gradient calibration, overall linearity, contrast, and signal to noise. The phantom and analysis software were designed by a collaborative group which included representatives from GE, The Phantom Laboratory, and the ADNI MRI core. The phantom can be purchased from The Phantom Laboratory. And the analysis software and service will be offered as a product by a newly formed company—Imaging Owl. A beta version will be available commercially the summer of 2006 and a fully tested product by the end of the year, 2006. ADNI has no commercial interest in the ADNI phantom, the analysis software for the ADNI phantom, The Phantom Laboratory, or Imaging Owl. The contact person for both the ADNI phantom and the analysis/service is Joshua Levy PhD, CEO of The Phantom Laboratory, at (levy@phantomlab.com).