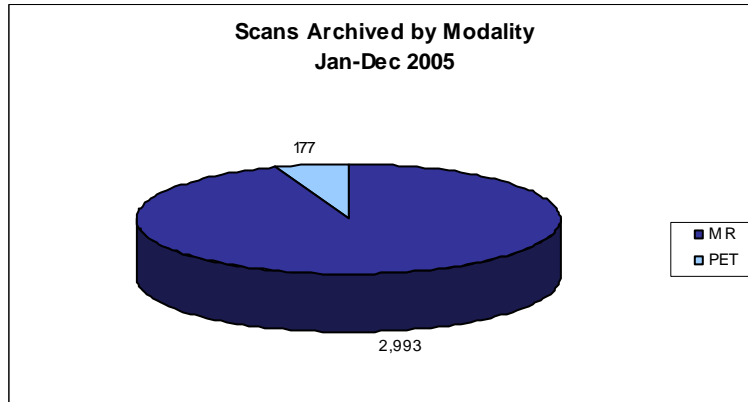


## ADNI Informatics Core 2005 Progress

The first full year of the ADNI project has been a busy one at LONI, resulting in a system which has been utilized by more than 100 users across 50+ sites. In all, more than 3,100 MR and PET images were archived in the LONI Image Data Archive in 2005.



The ADNI project has transitioned through four phases: Development Stage; Preparation Phase; Site Qualification Phase; and Execution Phase. Some of the significant efforts undertaken during each phase are described in the following sections.

### Development Stage

Initial efforts during the Development Stage focused on developing and validating de-identification programs suitable to the needs of the project, determining the specific needs of the ADNI Preparation Phase and developing plans to incorporate additional needed features. At the project's onset, IDA functionality included the ability to de-identify, transmit, store, query, collect and download imaging data in a reliable and HIPAA compliant manner. It was assumed that the data de-identification needs of the ADNI project would require customization to be compatible with the IRB language used by the participating sites.

The first steps toward developing the needed de-identification programs involved working with project leaders to establish an inventory of file formats expected to be archived. Since one goal of the ADNI project is to make data available to the general scientific community, it was necessary to craft a de-identification solution compatible with data sharing regulations and the goals of the ADNI. It was also necessary to ensure that appropriate data sharing language would be included in each site's IRB and consent documents. To that end, LONI provided suggested language for both.

Working with the MR core, custom DICOM de-identification programs were developed to remove/replace potentially patient-identifying information while preserving required information for each of the targeted MR scanner models (GE, Philips, Siemens). These programs were integrated into the IDA.

To support multi-site issues we:

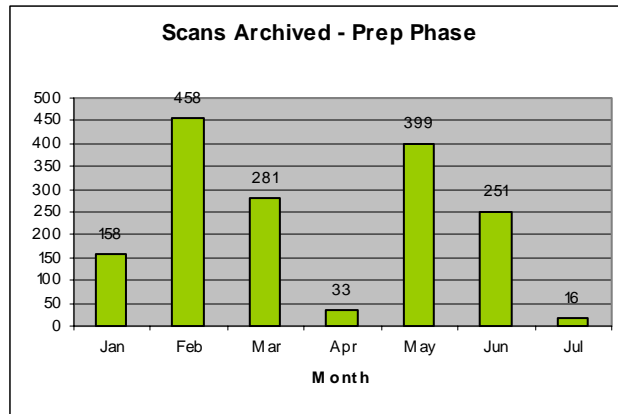
- Established a standardized subject identification convention. Building on our previous experiences we helped define an informative, non-patient-identifying subject identifier which was compatible with the image file formats.
- Created and distributed a sample Technical Manual to help highlight areas that typically need focus and standardization in multi-site projects.

## ADNI Informatics Core 2005 Progress

Once these issues were resolved, we coordinated user access and prepared to conduct a group telephone training session with all Preparation Phase participants.

### Preparation Phase

Five sites utilized the IDA to archive images acquired for the Preparation Phase. During this phase, 1,596 image series for 106 subjects were archived using approximately 45 Gigabytes of storage.



Shortly into the Prep Phase, it was determined that some system enhancements were needed:

- Information about the MR scanner coil needed to be displayed with the query results to support selection of appropriate scans. Determining the type of coil used for a scan is not readily apparent and the method for doing so varies across scanner models. It became necessary to enlist the help of many individuals in order to tackle this issue. System modifications were completed which involved further de-identification program modifications and changes to the IDA GUI.
- To improve system performance, new, faster and redundant servers were purchased and installed providing fail over reliability with near 24/7 availability. Considerable planning and preparation went into this activity and as a result, the amount of downtime was negligible.
- A customized [IDA User Manual](#) was developed and distributed.

During the same period, a comprehensive [ADNI website](#) was constructed (January of 2005). This site includes general information as well as sections pertaining to Research, Data Management, and insider information. The [Research](#) section includes the full ADNI grant application, a presentation section containing documents created from press conferences and ADNI meetings, and an extensive section on Research Cores with more than 40 documents on the GE, Philips and Siemens MR protocols. The [Data Management](#) section provides access to the ADNI Image Data Archive, provides statistics on the archived images, and is a repository for User and Technical Manuals. The [About ADNI](#) section provides general information on the ADNI project, an overview of Alzheimer's Disease and Mild Cognitive Impairment, an introduction to the core investigators, links to each of the site PIs and links to Steering Committee meetings. A restricted, password protected area of the section allows ADNI members to peruse Minutes from over 50 ADNI meetings and teleconferences. Information pertaining to the Research Cores, PET and Clinical Protocols, and an ADNI Community TWiki are also available through the restricted section.

In response to feedback from the Prep Phase users, a number of system modifications were implemented:

## **ADNI Informatics Core 2005 Progress**

- The ability to upload image files spread across multiple subdirectories to accommodate a wider variety of user situations was implemented.
- The speed of the upload process was improved and users were given the choice whether or not to compress their files during file transfer. A progress bar and a speedometer bar to indicate upload progress and network speed were also added.
- The ability to bypass the de-identification validation step, which decreases the amount of user interaction, was implemented.
- The organization of downloaded files was changed to be more user-friendly.
- The content of the query results was modified to provide more information about the MR scans such as the scan date, coil type and field strength.
- A document describing proposed user access levels/roles was distributed (attached).

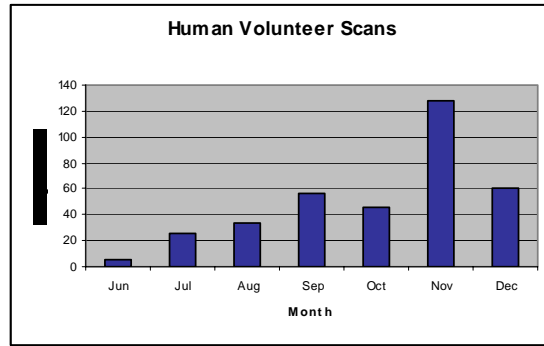
New functionality was created to meet the unique needs of the project:

- The ability to archive “synthetic” data required major modification to the system as the data were provided in Analyze format rather than in DICOM format as was planned.
- Validation of the user-supplied Subject ID was implemented to ensure that the Subject ID met the format defined for the project.
- The ability to download image data in file formats other than the original format (DICOM) was added providing users with greater choices when requesting data.
- An automated downloader program was created for use by the QC sites. The automated downloader queues all scans not previously downloaded and transmits them to the appropriate QC site when initiated by that QC site.
- To enable integration of quality control data between the QC sites, the ADCS and LONI, the LONI unique ID was adopted as the project-wide unique identifier for imaging data. Additional modifications were required to provide this information with each download.
- Programs to read/write and de-identify old-style DICOM were developed. There were a few sites that were using a deprecated form of the DICOM file format. Previous to this modification, these sites had to ensure the file extension was set to .dcm in order to archive scans in the IDA. After the modification they could simply upload without adding the file extension.

### **Site Qualification Phase**

As we progressed from the Preparation Phase into the Site Qualification Phase, the de-identification programs were further modified to accommodate additional requirements prescribed by the MR core. An ADNI Test project was established to provide users with a “scratch” area to practice uploading phantom images. As part of the Site Qualification Phase, each site was required to acquire and archive phantom and human volunteer scans. We contacted sites and conducted telephone training on the archival process. This effort often involved helping users install software and troubleshoot network and other computer-related problems outside the immediate scope of the IDA. In all, telephone training and support were provided to approximately thirty sites. During this process, 354 human volunteer MR scans were archived.

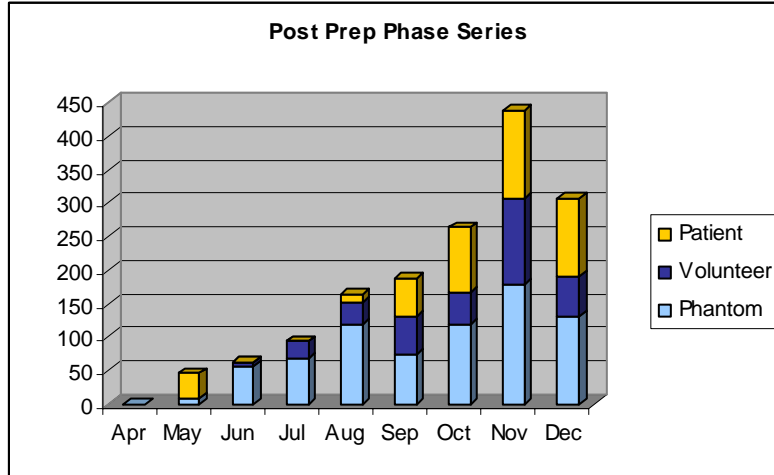
## ADNI Informatics Core 2005 Progress



As sample PET data became available, de-identification programs were prepared for the ECAT and HRRT file formats used for PET imaging. An additional step in preparing for the PET scans involved coordinating with the PET core in selecting metadata elements to be captured during the data archival process. Metadata elements are mapped from the image file headers into the IDA database to support queries. As each of the PET de-identification programs were completed, the relevant sites uploaded phantoms for site qualification. During 2005, 165 phantom PET scans were archived at LONI and transmitted to the QC site.

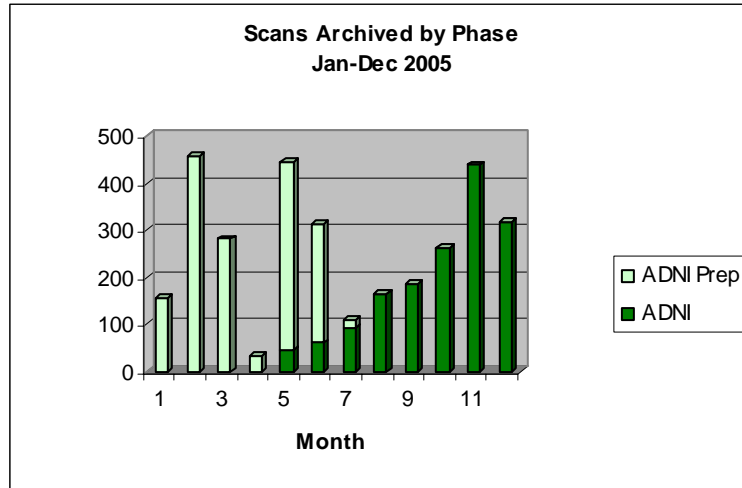
### Execution Phase

As we progress into the Execution Phase, we will continue to develop solutions to meet the evolving needs of the project. At year's end, 1,565 scans had been archived subsequent to the Preparation Phase.



From January through December of 2005, 3,170 imaging series were archived at LONI for all phases of ADNI, using more than 90 gigabytes of storage. More than 1,400 image series have been downloaded through the IDA in addition to the automated downloads transmitted to the QC sites.

## ADNI Informatics Core 2005 Progress



Throughout all phases, we have worked closely with the QC sites, assisted users at the acquisition sites, evaluated network issues, monitored the data archive and, when necessary, modified erroneous metadata elements and removed unwanted imaging data. Although the IDA User Management module allows project leaders at each site to administer user permissions, LONI now performs this role for all 50+ sites. To date, user permissions are being managed for more than 150 ADNI users.

In preparation for archiving processed data, we have worked with the QC sites and with the Voxel-based Morphometry group to assess needs in that area. A Processed Data worksheet was distributed as a way to collect information about the variety of processed data expected to be archived (attached).

We have been working with the QC sites and the ADCS group to develop solutions for integrating quality control information. As a first step toward addressing integrated, cross-database queries, we developed a simple prototype which was presented in September. We are developing components to allow archiving of processed data, and building support for data sharing outside the immediate ADNI community.



## User Access Levels

Access Level	Description
None	This is someone who has simply registered for a user account.
Archivist	This is often the MR or PET technologist, whose primary function is to upload scans into the IDA.
Guest	A guest is not formally affiliated with the project but is someone who would like access to information that is not generally available to the public such as the scan date.
Member	A project member is formally affiliated with the project. For example, an investigator at one of the analysis sites.
Manager	A manager is someone who has a primary role at one of the sites. For example, the site coordinator.
Leader	A leader is typically the PI or someone designated to act on behalf of the PI.

Function	Description
Basic Query	Query public access items (no subject IDs, dates)
Advanced Query	Query all items including subject ID and dates.
Upload data	Upload data into the IDA.
Public Download	Subject ID's are replaced & fuzzy dates substituted in the file header.
Private Download	Subject ID & dates remain in the file header.
Edit Metadata	Edit metadata (correct age, gender, etc).
Manage User Access	Grant access to other users.

	None	Archivist	Guest	Member	Manager	Leader
Basic Query	✓	✓	✓	✓	✓	✓
Advanced Query			✓	✓	✓	✓
Upload Data		✓		✓	✓	✓
Public Download	✓	✓				
Private Download		✓	✓	✓	✓	✓
Edit Metadata					✓	✓
Manage User Access						✓

ADNI  
VBM Processing Worksheet

Analysis Site	Process (Label)	Process (Description)	Program/Ver	Parameters	Data Type	ROI	Space	File Format	Tissue Type (G/W/CSF)?
UCSF	SNT	Semi-automated volume of the hippocampus, right and left	SNT	MPRAGE, atlas, landmarks	Volume	Hippocampus	Native	Analyze	
Dementia Research Centre University College London	Masking	This semi-automated morphological procedure aims to distinguish brain tissue from CSF, scalp and other non-brain tissues. It creates a binary mask which includes grey and white matter, cerebellum and brain stem (as low as the lowest extent of the cerebellum) as well as supra-tentorial structures. It excludes ventricles as well as sulcal CSF. The cut-off between CSF and grey matter is inevitably arbitrary because of partial volume effects; in order to maximise consistency an intensity cut-off (which is a fixed percentage of mean brain tissue intensity) is used (e.g. voxels that are <60% of mean brain intensity are considered CSF and are excluded).	MIDAS Freeborough PA, Fox NC, Kitney RI. Interactive algorithms for the segmentation and quantitation of 3-D MRI brain scans. Comput Methods Programs Biomed. 1997; 53:15-25	Percentage of mean brain intensity used to delineate brain from CSF (60-160%)	Mask	Brain	Native	Analyze	
UCLA	9-parameter registration of follow-up to baseline	9-parameter alignment transformation matrix that aligns follow-up scan to baseline scan	minctracc	MI option, lsq9 matrix	matrix	n/a	Follow-up	.xfm	
	9-parameter registration of baseline to standard ICBM space	9-parameter alignment transformation matrix that aligns baseline scan to a standard space (ICBM53 space for us)	minctracc	MI option, lsq9 matrix	matrix	n/a	Baseline	.xfm	
	Jacobian Map	Map of the Jacobian determinant (i.e. atrophy map) in the same space as the baseline scan	Inv Consistent Elastic Warp	Intra-subject Defaults	Volume	All of ICBM space	ICBM baseline	Analyze	
	Nonlinear Warp over Time	Vector field applied to the follow-up to deform it to the baseline, all after linear registration to standard ICBM52 space	Inv Consistent Elastic Warp	Intra-subject Defaults	3 Volumes, DX, DY, DZ	All of ICBM space	ICBM follow-up	Analyze	
	Nonlinear Warp to Standard Subject	Vector field applied to the Jacobian map to convect it from baseline ICBM space to a nonlinearly registered space	Inv Consistent Elastic Warp	Inter-subject Defaults	3 Volumes, DX, DY, DZ	All of ICBM space	ICBM follow-up	Analyze	
	Baseline Image used	Saved so it is always possible to check which orientation the processed image was in, after N3	N3	Defaults, with ICBM mask	Volume	Whole brain	Native	Analyze	
	Follow-up Image Used	Saved so it is always possible to check which orientation the processed image was in, after N3	N3	Defaults, with ICBM mask	Volume	Whole brain	Native	Analyze	

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ADNI  
VBM Processing Worksheet

Analysis Site	Process (Label)	Process (Description)	Program/Ver	Parameters	Data Type	ROI	Space	File Format	Tissue Type (G/W/CSF)?
Arizona	Spatial normalization templates and customized g/w/csf priors for segmentation	Templates from samples of ADNI participant scans selected to be proportionally representative of the subject groups and acquisition sites for the whole project sample and matched on distributions of demographics will be created with SPM2 for baseline and longitudinal analyses	SPM2 (note: may switch to SPM5 when released and tested)	Defaults modified with voxel dimensions	Volumes	whole brain, and segmented gray matter, white matter and CSF maps	Sample-specific template space	Analyze	Gray/White
	Parameter files for spatial normalization to templates	Files of coefficients (DCT and 12 parameter affine) to transform baseline and combined baseline and longitudinal scans into sample-specific template space	SPM2	Defaults	matrix	n/a	Sample-specific baseline and	Matlab	n/a
	linear affine alignment of	Registration of follow up scan to baseline scan for longitudinal comparisons	SPM2	Defaults and modified for 9 parameter	matrix	n/a	Native	Analyze; text file	n/a
	Jacobian determinant	Jacobian determinant obtained from high deformation spatial normalization of follow up scan to baseline for longitudinal analyses	SPM2 and high deformation toolbox	Defaults	Volume	Brain	Native baseline	Analyze	n/a
	Cross-sectional baseline	Baseline scans smoothed after normalization and segmentation for cross-sectional analyses	SPM2	Defaults	Volume	Brain segmented for	Sample-specific	Analyze	Gray/White
	Longitudinal baseline and follow up normalized, segmented, and smoothed images	Baseline and follow up images smoothed after normalization and segmentation for longitudinal analyses; includes high deformation spatial normalization of follow up to baseline scan after linear affine alignment	SPM2	Defaults	Volume	Brain segmented for gray and white matter	Sample-specific template space	Analyze	Gray/White
	Statistical results files	Post-script files containing results and design matrices for cross-sectional and longitudinal statistical comparisons; t and F map image files; brain mask for statistics; contrast files; variance map image files; and statistical settings in matlab	SPM2	n/a	figures/text/volumes	n/a	Sample-specific template space (kewei)	post-script/analyze/matlab	Gray/White