I Morphometry BIRN: Annual NCRR Progress Report

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II Narrative Description

A Project Overview

The overall goal of the Morphometry BIRN (mBIRN) project is to develop, test and disseminate an infrastructure that enables a clinical research scientist to seamlessly acquire, share, analyze and mine multi-site data derived from structural MRI, diffusion MRI and clinical data, using processing and visualization tools developed at multiple sites. An excerpt from the October 2004 Competing Renewal Overall Narrative is included in the Appendix stating the Core Project goals (section A). The Appendix also includes a table (section B) that outlines the participating sites with their personnel and roles.

B Project Focus

The goals of development, testing and dissemination define the focus of the mBIRN work:

Domains of Technology Development

- Standardized MRI acquisition protocols and image calibration methods for multi-site structural and diffusion imaging.
- Integration of visualization and morphometric analysis software developed at different sites to seamlessly interchange relevant data inputs and outputs. Software includes brain segmentation, shape analyses, diffusion analyses, integrated visualization, query atlas and machine learning tools.
- Computational informatics framework that enables curation, data management (raw MRI, derived morphometry data, clinical assessments, demographics) and computational workflows for a well-controlled way of generating and tracking provenance of derived data.

Prototype Application Tests

We have defined prototypical clinical research studies that require exactly those technologies we seek to develop. These prototype application tests use valuable, existing legacy data (neuroimaging and clinical) and/or software tools (visualization and morphometry) from multiple BIRN sites to address specific research issues in the study of ageing and Alzheimer's Disease and Depression. Some application tests involve our non-BIRN Collaborators. These application cases enable validation of the technologies as well as dissemination by means of peer-reviewed publication of novel findings and methods that would not be possible without the BIRN **(see section II.E)**.

Dissemination

The ultimate goal is to disseminate and support the validated technologies for the clinical research community. The BIRN recommendations for MRI acquisition protocols are posted on the mBIRN website. As much as possible software developments are based on standards and open source code. Completed software code will be distributed from the BIRN Portal and websites of the participating sites to enable tracking of the reach of the tools and infrastructure. Benchmark data sets (e.g. from the traveling human phantoms used in the MRI calibration studies) will be de-identified and made available to the scientific community for use in algorithm development.

C Progress Highlights

Below are highlights of some mBIRN projects. More details can be found from the presentations given by the Core Projects at our recent mBIRN Annual Meeting (March 2-4, Miami, http://www.na-mic.org/Wiki/index.php/Summary_Progress_Reports).

C.1 Technology Developments

- **Multi-site MRI acquisition and calibration methods**
  - Distortion corrections in structural MRI: We have completed the validation that our gradient non-linearity distortion correction algorithm reduces image distortions and improves test-retest reproducibility of image intensity in multi-site structural MR data studies. The results are described in a manuscript that we intend to submit to NeuroImage in April 2005. The manuscript will also point readers to a website from which the distortion correction open source code with documentation can be downloaded.
  - Distortion corrections in diffusion MRI: The Duke site has completed the validation of a method that significantly reduces distortions in diffusion MRI data, and a manuscript has been submitted to NeuroImage (see abstract in section **III Appendix C**). Although this work pre-dates Morphometry BIRN, it is expected that it will reduce variability in multi-site diffusion studies. The method, originally implemented on a GE platform, is currently being ported to other platforms for multi-site tests (Philips at JHU, and Siemens at MGH).
- **Validation of MRI defacing software**
  We have completed development of a de-identification process for imaging data that includes stripping all identifying information from the header files and removing facial features from the image data to enable HIPAA compliant MRI data-sharing. The defacing tool is an extension of the morphometric analysis software, Freesurfer, developed at the MGH site. The validation of the defacing algorithm needs two independent tests before it can be disseminated: a) demonstration that the algorithm leaves the brain untouched and thus defaced data can be used for morphometry, and b) demonstration that defacing effectively removes a subject's identity. Both of these tests are in progress and are expected to generate separate manuscripts. More details on the defacing work can be found at: http://www.na-mic.org/Wiki/index.php/Defacing
- **MRI skull stripping comparison study**
  Morphometric analysis of large-scale data sets requires robust, automated methods for pre-processing of the data, including skull stripping. A study that assessed the four different skull-stripping methods in most common use, several of which were independently developed at mBIRN participating sites, has been completed. The study focused on the implementation of the software tools on both healthy control and neuro-psychiatrically diseased brains, an extension rarely seen in the literature on this topic, but critical for the advancement of structural MRI as an outcome biomarker for clinical studies. The manuscript reporting these results is in press in Human Brain Mapping (see **section II.E**).
- **BIRN De-identification and Upload Pipeline (BIRNDUP)**
  Additional progress has been made during the reporting period on the application of mBIRN-developed tools outside of the original mBIRN collaboration group. In particular, the National Alliance for Medical Image Computing (NA-MIC) National Center for Biomedical Computing (NCBC) (see **II C.3. Collaborations** section below) has been testing the defacing and DICOM de-identification tools embedded in the BIRNDUP software to enable data sharing within this new project group. High-resolution T1 (SPGR) images from Dartmouth-Hitchcock Medical Center's Brain Imaging Lab were successfully run through BIRNDUP processes. Dartmouth is currently reviewing

the results to confirm that the algorithm leaves the brain untouched. The results from their feedback along with the outcome of the defacing studies described above will be used to do any final improvements in this software prior to dissemination to the scientific community.

- **Diffusion Tensor Imaging Analysis**

  Diffusion Weighted Imaging (DWI) and Diffusion Tensor Imaging (DTI) are newly added to the mBIRN aims as part of the current reporting period. The goal is to create an integrated set of tools for visualizing and analyzing diffusion MRI and derived data, integrating both data and tools from multiple-sites. The first efforts in this domain have been to collect a set of representative DWI/DTI data sets from several of the collaborating sites in order to capture the variation of file formats and acquisition protocols present at the sites. New input libraries have been created for the mBIRN visualization software, 3D Slicer, to support slice interleaved, volume interleaved, and mosaic file types. In addition, the readers are now configurable to support any number of baseline and gradient DWI images. These changes allow us to perform tractography and related DTI analyses on a wide variety of data sources, including the DTI images acquired at UCI for use in the creation of White Matter Atlases by Jim Fallon (UCI), and the DTI data collected as part of the VETSA study (see **II C.3. Collaborations** section below). In addition, a label map-based editing tool for doing region-of-interest (ROI) analysis of tractography has been implemented in 3D Slicer to support the creation of White Matter Atlases.

- **Quality Assurance Tools**

  Most segmentation tools require human interaction with intermediate or final results for quality assurance (QA) purposes. Having efficient QA tools can save considerable technician's time and increase analysis throughput. A new set of custom-configured QA review tools have been added to 3D Slicer to facilitate the rapid review of FreeSurfer generated derived subcortical segmentation data sets as required by large cohort studies exemplified by the Multi-Site Alzheimers Disease (MAD) study (see **II C.2 Application Tests**). This tool simplifies the tasks related to expert investigator review of automated registration and segmentation results.

- **Large Deformation Diffeomorphic Metric Mapping (LDDMM) code optimization**

  The programs used for shape analysis (LDDMM source code, from JHU), have been optimized, resulting in a 30 % reduction in time for a shape comparison of two human hippocampi. LDDMM has also been modified to allow users to save a subset of output data (to save storage space).

- **Data management tools**

  Our overarching goal in the development of the data management infrastructure is to ensure efficient, reliable and dynamic access to neuroimaging and neuropsychiatric data at all stages of the research process. While this overall goal encompass many technical areas, we have focused on the development and distributed deployment of database tools to support local and global access, frameworks for ontological description of information to facilitate data integration and knowledge management and exploration, and development and integration of data provenance into the processing and storage of derived information. Our progress since October 2004 in these key areas is summarized in the following sections.

  - Database Systems: We continue our work on the development, local testing, and deployment of three solutions for local image data management: the BIRN Human Imaging Database (HID), XNAT, LONI-DB. Each of these systems has various strengths that will appeal to the broader scientific community. HID has the broadest mBIRN involvement in development. Efforts are focused on improving functionality and deployment procedures, using other mBIRN and fBIRN sites as beta testers and documentation development. Particular effort has been devoted to facilitate entry of non-imaging metadata (such as behavioral and clinical assessments) through the

use of an integrated set of web-based form creation, deployment, and database-integration tools. To date, 10 commonly used clinical assessments have been incorporated using this system. XNAT, a comprehensive data management suite developed at the Washington University site prior to their BIRN participation, is currently in beta-test for distributed deployment with an initial site (MGH). Deployment scripts and documentation are developed, and experience with the problem of individual-site data model generation has yielded refinements in the system. Upon successful installation at MGH, the beta-test will be opened to additional mBIRN and other sites.

- Provenance: The purpose of the provenance effort is to facilitate the recording of a comprehensive history and version information for processing tools used in the mBIRN project in order to allow the recreation of derived data. To date, we have completed the specification of a general provenance XML schema, which has been implemented in a number of the processing tools in the mBIRN data analysis processing streams. In addition, it has been integrated with the HID database schema. This effort is on going with plans to bring all mBIRN developed analysis tools into compliance with this requirement (http://www.na-mic.org/Wiki/index.php/Data_provenance).
- Semantic Web and Ontology: The goal of this effort is to create an ontology prototype that relates brain structure and function through neuroanatomical regions, neuropsychological and cognitive terms, and clinical assessments, and semantically aware tools to navigate this (and other) information. Numerous tools are now available within mBIRN to be utilized in this effort including: KNOWME and BONFIRE – tools to aid the integration of electronic biomedical information from a variety of sources and to make it easy for users to link disparate information systems; Haystack (as well as Hayloft) - a Semantic Web browser that aggregates RDF (define this or cut it) from multiple arbitrary locations and presents it to the user in a human-readable fashion; PIGGY-BANK – an extension designed to let web browser collect and browse "semantic data" linked from ordinary web pages; and Platypus - a “semantic WIKI,” that allows relational links between objects and the creation of new terms. Efforts are underway to uniquely utilize the existing efforts embodied in BONFIRE and the UMLS, with additional terms and concepts from the anatomical and psychological domains (i.e. American Psychological Association Thesaurus). Also, a web-service has been developed that facilitates the conversion of terms from various source ontologies and facilitates tool interoperability. More details can be found in: http://www.na-mic.org/Wiki/index.php/Ontology.

- **Data processing workflows**

  As mBIRN image acquisition, analysis and interrogation resources have matured the need to tie them together has evolved as an mBIRN-wide focus. The use of a well functioning image analysis pipeline will facilitate not only the initial calculation of the experimental results, but also the recalculation for verification of the results, and the exploration of the results.

  Analysis pipelines require unifying image data processing standards, file formats and provenance at mBIRN sites to become single, harmonized mBIRN solution. The benefits of a single mBIRN analysis pipeline solution are that it will allow i) collaborations between sites to be set up faster, ii) greater exploration of recalculated experiments and iii) the ability to routinely explore complex parameter spaces. Initial requirements for an mBIRN pipeline solution will be to build a completely open source solution based upon existing workflow expression standards with an architecture that can support current mBIRN use-cases (SASHA, MIRIAD, and MAD, as described in **section C.2. Application Tests**). Analysis pipelines have been developed at several mBIRN sites; however there has not been an mBIRN-wide open source solution. We are currently working to define an open source language specification that supports our long-term goal of a unified mBIRN pipeline but also that conveniently maps to the existing pipelines developed over the years at the mBIRN sites.

Our progress since October 2004 has been mainly on three fronts: i) identifying potential candidates of open source pipeline specifications and in gathering more specific information about the existing mBIRN pipelines, ii) designing a general mBIRN-wide pipeline architecture, and iii) continue developments and improvements of the LONI pipeline (UCLA).

- Pipeline Language Specifications: We will attempt to combine the various parts of the analysis pipelines that have been used to date, either at the level of specifications or code. At the level of specifications, the requirements for these are expressed as a pipeline definition language. Since analysis pipelines in science are roughly equivalent to workflow definitions in business, we are also looking to business for workflow specifications. In business, as in science, workflow definition languages are used to embody the requirements for the workflow applications. Current business workflow languages that appear to embody some of our requirements are the XML Process Definition Language (XPDL, sponsored by the Workflow Management Coalition) and the Business Process Execution Language for Web Services (BPELWS, sponsored by a coalition of BEA, IBM, Microsoft, SAP AG and Siebel Systems). Scientific analysis pipeline languages that appear to embody some of our requirements include XML Simple Conceptual Unified Flow (XScufl, sponsored by the myGrid project), Modeling Markup Language (MoML, sponsored by the Kepler project), and Laboratory of Neuro Imaging XML Workflow Representation (LONI-XML, sponsored by the Laboratory of Neuro Imaging).
- Architecture: The requirements of the pipeline will be defined to a great extent in the XML specification of the workflow. The agreement to work on this XML specification was made at the March 2005 mBIRN All Hands Meeting. The evolving architecture of the actual workflow application will be described in the section on future directions. However, the adoption of existing applications (such as the LONI pipeline) as a starting point to build the architecture is highly desirable. The architecture later described would then be layered upon the existing application and evolve in an mBIRN open source setting.
- LONI Pipeline: Ongoing developments on the data processing LONI pipeline have led to publications that validate its use as a processing and visualization environment that can facilitate neuroscience research (see **section II E Publications**). There has been significant work on a major new pipeline release (http://www.na-mic.org/Wiki/index.php/LONIPipelineSummary).

C.2 Applications Tests

- **Semi-Automated SHape Analysis (SASHA)**

Background: The SASHA is a collaborative application aimed at developing a morphometry pipeline that integrates subcortical and shape analyses using tools developed at different sites. Clinical imaging data acquired at one site (WashU) is being analyzed by morphometry tools from two other different sites: Freesurfer subcortical segmentation at MGH followed by shape analysis (Large Deformation Diffeomorphic Metric Mapping, LDDMM) at JHU. A visualization tool from a fourth site (BWH) has been extended to enable the viewing of all the derived results on a single platform. To drive the integration of the pipeline preliminary data from R. Buckner (WashU) were analyzed (45 subjects: 21 nondemented controls, 18 very mild Alzheimer's Disease and 6 semantic dementia).

Progress: Main progress fronts include: i) preliminary validation of the SASHA pipeline for clinical diagnostic use, and ii) use of the Teragrid to facilitate computations and data handling originating from LDDMM analyses. These are outlined below.

i) A novel statistical analysis method has been developed and tested that seems to provide accurate classification of subjects by disorders from LDDMM metric distances. These results are summarized in a Human Brain Mapping abstract (**see section II.E**)

ii) The TeraGrid (www.teragrid.org) computational resource was used to facilitate the LDDMM processing. The 32K cpu/hr processing time was distributed among 3 TeraGrid sites NCSA, CalTech and SDSC. Each site had local restrictions on the number of submissions to their resources. A meta-scheduler does not exist to submit all 4050 LDDMM jobs. Human intervention was needed to load, balance and monitor processing activities. Data results were automatically stored on BIRN repositories through the use of the Storage Resource Broker.

- **Multi-Institutional Research in Analysis of Depression (MIRIAD)**

  Background: The MIRIAD is a collaborative application aimed at developing a morphometry pipeline that integrates multi-site neuroimaging analysis tools that process MRI data typically acquired for detecting white matter lesions (T2- and proton density MRI). To drive the application we attempted to extend the analysis of retrospective depression data from the Duke site, which had been previously analyzed using only manual segmentation methods. This data was further processed using registration, atlas generation and segmentation tools from the BWH and UCLA sites.

  Progress: A first validation of the MIRIAD pipeline on the depression data has been completed and the results have been submitted as a manuscript (see abstract, **III Appendix C**).

- **Multi-site Alzheimer's Disease (MAD) project**

  Background: It is expected that pooled analysis of multi-site data from prospectively collected data, such as that from the Alzheimer's Disease Neuroimaging Initiative (ADNI, see **II C.3. Collaborations** section) will be successful since the acquisition and calibration methods will be tailored for this aim explicitly. However, many research groups have valuable legacy data sets that have been collected using best available methods for their site. This study will test the hypothesis that such legacy collections of clinical and structural MRI data from different sites can be meaningfully reanalyzed as a larger combined data set by using rigorous data curation and image analysis methods. We will explicitly test the hypotheses that hippocampal volume, as measured by the Freesurfer segmentation algorithm, will show the expected age related volume decrease, sex effect and laterality, as well as atrophy correlated with cognitive decline as measured by Mini-Mental Status Exam (MMSE) and diagnosis as measured by their Clinical Dementia Rating (CDR) score using data collected for studies of AD, Minimal Cognitive Impairment (MCI) and normal ageing at five mBIRN sites (UCSD, UCI, WashU and MGH/BWH combined).

  Progress: In the initial years of the mBIRN, the legacy data from the UCSD and MGH/BWH sites were used to develop a prototype demonstration while the image analysis software was being enhanced to work optimally on these legacy data sets. Enhancement of the analysis software required manual segmentation of representative data sets for the creation of a training atlas, improvements of the skull stripping and image registration algorithms as well as development of an algorithm to estimate total intracranial volume from the T1 images for normalization purposes. We have just completed the Freesurfer segmentation of over 280 total data sets from the contributing sites. Our preliminary analysis shows that the significant site difference in hippocampal volume in the healthy control subjects was a consequence of the variations in image processing which we have now eliminated. Final data curation of the clinical data (age, sex, diagnosis, education, and MMSE score) and Freesurfer analysis results is now underway. (See http://www.na-mic.org/Wiki/index.php/Multi-site_AD for more details).

  Of note, this study has been a key prototype for the development of the infrastructure for 1) data sharing across sites that followed federal HIPAA guidelines for de-identification (Defacing, BIRNDUP code), 2) common database schema for clinical and derived morphometry data at each site and a Mediator to bring the multi-site information together seamlessly (HID), 3) shared locations

for data storage and retrieval (Storage Resource Broker), and 4) mediated queries that interrogate data contained in databases located at the two sites (HID Query Interface, 3Dslicer, Query Atlas).

C.3 Collaborations

The mBIRN is collaborating with multiple local and nation-wide projects. Besides our publications, these collaborations currently are the main method for disseminating and optimizing mBIRN tools and protocols. We highlight here a few selected collaborations.

- **Alzheimer's Disease Neuroimaging Initiative** (ADNI, http://www.loni.ucla.edu/ADNI)
  The ADNI is a multi-institutional effort to find neuroimaging and other biomarkers for the cognitive changes associated with Mild Cognitive Impairment and Alzheimer's Disease. It is funded with the provision that all collected data must be shared with the broad research community, thus is closely aligned with the mBIRN goals and mission.
  We collaborate closely with the ADNI Neuroimaging Core to support and assist them in their multi-site calibration of structural MRI data for brain morphometry. The acquisition protocols and correction methods that they are testing include those proposed by mBIRN, and will enable testing at over 40 sites. The evaluations of these methods on patients with MCI and AD will help establish the clinical relevance of the calibration methods.

- **National Alliance for Medical Imaging Computing** (NA-MIC, http://www.na-mic.org)
  Supported by the NIH Roadmap Initiative for Bioinformatics and Computational Biology, NA-MIC is a multi-institutional, interdisciplinary team effort to develop novel algorithms and open source software engineering technologies for the analysis and visualization of medical image data. NA-MIC has central goals for training and dissemination of these tools to the medical research community. Where BIRN's emphasis has been on application and adaptation of existing image analysis techniques to a distributed grid-computing environment, NA-MIC participants are committed to extending the mathematical underpinnings of medical image analysis and converting these new techniques into deployable software solutions. In keeping with their distinct mandates, BIRN and NA-MIC collaborate closely on several fronts: i) data acquisition and analysis: both NA-MIC and mBIRN have key deliverables in the domain of DTI data. MBIRN is providing key support to NA-MIC for acquisition, calibration and distortion correction methods, ii) data visualization: a key visualization software platform developed at the NA-MIC PI site, 3D Slicer, is being further developed under the auspices of both mBIRN and NA-MIC to vastly expand the capabilities of this versatile software tool, iii) BIRN is providing the secure data hosting facilities and Internet2 infrastructure to support the nationally distributed team of NA-MIC developers and end-users, iv) training and dissemination: members of the mBIRN MRI Calibration Core (A. Song from Duke, and S. Mori from JHU) have agreed to provide software tools and expertise to NA-MIC for development of educational materials (tutorials and other interactive, web based learning tools) for DTI data acquisition and data analysis. Further, the data collected by the mBIRN Calibration core will be made available for use in this educational material.

- **Vietnam Era Twin Study of Aging (VETSA)**
  The VETSA is a multi-site (UCSD and MGH) longitudinal (5 year) study in which neuroimaging, neuropsychology, clinical assessments and genetic data is being collected from Vietnam-era (male-male) twins (n=300 pairs, half at each site) to study normal ageing.
  Our collaborations with the VETSA project are two fold: i) the MRI acquisition protocols and correction methods used by VETSA include those proposed by mBIRN, so they will offer additional validation and optimization, and ii) the VETSA diffusion MRI data is being analyzed using software tools developed at mBIRN sites (white matter atlases generated by S. Mori at JHU and D. Kennedy at MGH, and also diffusion tensor registration tools from S. Pieper at BWH).

- **Function BIRN**
  The Morphometry and Function BIRN testbeds have worked together closely on several fronts, here we highlight just a few:
  - High field morphometry calibration: mBIRN has performed the cortical and subcortical segmentations and surface reconstructions of sample structural MRI data acquired as part of fBIRN's Phase II acquisitions in the Minnesota site (Siemens 3T). Qualitative inspection of the results shows that accurate segmentations were possible with the current acquisition protocol. The next step is to process high field sample data sets from the other fBIRN sites.
  - Imaging genetics: Analysis efforts of imaging and genetics data have resulted in a paper in submission to Neuroinformatics (see section **II E Publications**). Dr. Smyth and Dr. Fallon are developing mathematical frameworks and neurocircuitry arguments, respectively, for datamining large datasets such as those being collated by mBIRN.
  - BIRN-GCRC Interactions: Together with BIRN CC, GCRC and NCRR we have selected pilot short-term collaborative projects with three GCRCs. The main goal of these collaborative projects is to disseminate tools and experience in both directions. The GCRC's are:
    - *Medical College of Wisconsin* (Steven Rao): this collaboration has two components: a) use of fBIRN's stability assessment phantom, protocols and analysis tools at MCW and b) use of a rich fMRI dataset from MCW to drive fBIRN analysis tool development.
    - *University of Texas* (Peter Fox): this collaboration involves sharing and expanding the taxonomy for neuroimaging databases developed by both groups.
    - *Brigham and Women's Hospital* (Gail Adler and Reisa Sperling): The collaboration with G. Adler is to enhance their cardiac image analysis tools using co-registration tools originally developed for brain applications. The collaboration with R. Sperling involves cross-site calibration of both functional and structural MRI for studies of AD.

C.4 Project Management

Through our collaboration with the NA-MIC, we developed Wiki pages for the Morphometry BIRN project (http://www.na-mic.org/Wiki/index.php/Mbirn:Main_Page). This system is meant to encourage quick and efficient communication among the participating investigators and the interested users. The Wiki pages are easy to use and help distribute the task of documenting progress and interactions across the various working groups. The Wiki pages proved to be useful for our Annual Morphometry BIRN meeting (Miami, March 2-4, 2005), enabling us to easily and quickly update our agenda and distribute the summary notes and presentation materials, before, during and after the meeting.
The Wiki pages are currently completely open: anybody can read them or update them. Upon our request, BIRN CC is exploring how to set up password protected Wiki pages on the BIRN Portal. The tool will potentially then be adopted by the other testbeds.

D Outline of future goals

D.1 Technology Developments

- **MRI Calibration**
  The future goals for the MRI Calibration efforts are organized around the deliverables for Oct 2005, which include (http://www.na-mic.org/Wiki/index.php/Goals_for_MRI_Calibration):
  - *Acquisition Protocols*: We will maintain and update on our BIRN website (mirrored on web sites of mBIRN participants) MRI acquisition protocols for all major vendors and field strengths for T1, T2, PD and Diffusion imaging. We will use our research agreements with

MRI vendors to facilitate sharing state of the art acquisition protocols across sites through 'works in progress' packages.

- *Software Correction Tools*: Our target is to have the following two open source tools available by Oct 2005: gradient unwarping distortion correction and Bo + Eddy current correction code.
- *Validation (quantitative analyses, publications)*: the main three working fronts include validation of the multi-site acquisition protocols and correction methods for:
  - Multi-spectral T1-weighted MRI: this will be mostly driven by our collaborations with the ADNI project
  - Multi-spectral T2-weighted MRI: this will be driven by test-retest acquisitions of lesion data at Duke from 2 patients and preliminary quantitative evaluation of lesion detection reproducibility
  - Diffusion MRI: the acquisition protocol optimizations for effective reproducibility of diffusion-derived data will continue at JHU. The distortion correction efforts will continue with the implementation and testing of Duke's GE methods on JHU's Philips system.

- **Analysis, Visualization, and Interpretation (AVI) Aims**

  Ongoing efforts underway at mBIRN sites to address the sub aims associated with AVI projects:

  - MBIRN protocol-specific cortical and subcortical segmentation efforts are focused on the refinement and validation of Freesurfer software tools to operate efficiently using the next generation of acquisition protocols that use Multi-Echo Flash (MEF) imaging. We are also working on license issues to release open source code.
  - MBIRN protocol-neutral segmentation efforts are being augmented by the addition of an integrated segmentation and registration tool being developed at MIT and BWH through a collaboration of mBIRN with NA-MIC. This integrated framework has been developed to address shortcomings with the traditional approach in which registration of population-based atlas data is performed solely on the basis of image metrics on the raw image data. The new method, in contrast, allows calculation of an affine transformation for each substructure in the segmentation hierarchy as part of the optimization loop for the segmentation. The use of the segmentation tissue model appears to improve the registration while avoiding errors. In addition, optimization of the segmentation techniques for automatically identifying white matter lesions are continuing in collaboration with the BWH Center for Neurological Imaging, a center with significant expertise in processing of Multiple Sclerosis (MS) data. The collaboration with CNI is anticipated to result in improved algorithms for mBIRN use on depression data sets and further MS applications.
  - Shape Analysis plans include the specification of an mBIRN HID table to capture the results of large-scale shape analysis being performed on the TeraGrid using the JHU-developed LDDMM tools. With the addition of 12T of dedicated disk space, the project will make better use of the BIRN clusters being brought on line by BIRN-CC.
  - Diffusion processing efforts will continue to emphasize interoperability with images acquired across multiple sites, augmented by the distortion correction tools being developed in the calibration Aims of mBIRN. These uses of these tools will support the creation of white matter atlases and detailed white matter analysis of individual subject data sets.
  - Integrated Visualization and Query Atlas aims are supported by further development of the 3D Slicer application framework, with the significant efforts being placed on creation of a dedicated QueryAtlas Module in 3D Slicer as a focus point for code that has to date been

included in several different portions of the source code. This refactoring will allow faster development of new QueryAtlas functionality with a more object-oriented design.

- Machine learning efforts will focus on joint work between MGH and MIT to apply automated clustering to longitudinal hippocampus volume assessments being generated using the FreeSurfer tool in the MAD data sets (see **section II C.2 Application Tests**). With this analysis as a reference point, the machine learning tools will be integrated into a format compatible with the BIRN Portal for use on a wider range of mBIRN data.

- **Data management tools**
  Ongoing developments are underway at mBIRN sites to address the sub aims associated with the data management project:
  - XNAT Developments: Demonstration of BIRN interoperability by importing sample BIRN data into XNAT database via BIRN data XML export; explore XNAT - BIRN schema and data model relationships and interoperability; establish homologies between schemas; with clinical collaborators, develop query interface improvements and user configuration; implement user-based roles and groups to facilitate controlled data sharing; deploy and establish use at ~3 sites (WashU (already), MGH, other to be designed).
  - HID Developments: Add the Clinical Assessment Layout Manager (CALM, a tool for data entry) into HID graphical user interface; with clinical collaborators, develop query interface improvements and user configuration.
  - LONI-DB: Deploy and make fully operational at ~2 sites (UCLA (already), MGH)
  - Provenance Developments: store provenance data in databases (XNAT, HID); develop query-by-provenance tools in databases and in BIRN Portal
  - Ontology: Compile a formal anatomic, behavioral, and clinical ontology prototype; develop the means for community group collaboration and discussion of these ontologies; expose relevant portions of UMLS for semantic web exploration using MIT's Haystack tool for having an organized user's interface based on specified relationships.

- **Data processing workflows**
  The goal is for a workflow analysis pipeline application suite to evolve that will encapsulate the mBIRN image processing requirements. Ongoing and future work involves:
  - Definition of specifications: The application suite should be open source and highly conducive to loosely coupled development between teams of programmers. The core applications should be platform independent to the extent that they should run on Windows and Linux platforms. To that end, the programming languages used in the core of the program will be Java and C++. However, the architecture will be primarily based upon the use of web services, and these web services can access programming in any language and on any platform that has a web server available.
  - Definition of pipeline architecture: The resulting analysis pipeline will be defined in the context of 4 available services. Data such as images and patient demographics will stream though the pipeline. This data is processed through a series of programs, which constitute the analysis pipeline. The core pipeline management software application will manage theses applications, and be responsible for directing the data to the applications in a secure manner, recording the application versions that are used, providing uniform error trapping, providing a quality assurance strategy, providing a standard recovery on failure, and providing a central metadata repository for tracking the jobs. Data provenance will be recorded through the pipeline services.

The pipeline architecture will allow loose coupling to existing programs. It will be possible to run existing applications locally if they exist on the client machine with the appropriate API's to the pipeline core application. However, through a Service Oriented Architecture (SOA), applications will be able to run on distant machines using a SOAP interface. Polling of specific unified resource locations for available applications (resource discovery) will be part of the core pipeline architecture. With this architecture, mBIRN will provide a specification for building an application for data analysis that can be run as a service. These applications could then be discovered and run by the pipeline. This provides a good way to enable concurrent development of resources in this loosely coupled framework.
(More in: http://www.na-mic.org/Wiki/index.php/MBIRN_Pipeline_Arquitecture_concept)

- LONI Pipeline: new release is currently being tested and evaluated and we plan to release in June 2005.

D.2 Application Tests

- **Semi-Automated SHape Analysis (SASHA)**
  The short-term future plans include:
  - Test that the promising results that allowed us to define reliable metrics for classifying subjects by disease can be reproduced with a new dataset. To accomplish this, a new dataset from R. Buckner (WashU) will be processed through the SASHA pipeline. This dataset consists of 50 young controls, 50 old controls and 50 AD (50/50/50). The expectation is that the results will be reproducible and that a manuscript will be prepared on this new analysis method for characterizing disease from morphometry data.
  - The reproducibility study will drive the continuation of large-scale testing for SRB with BIRN CC (optimizing SRB structures to enable representation of multiple LDDMM runs with varying parameters) as well as the study of algorithm optimizations for LDDMM analyses.
  - Continue working with Mouse BIRN to determine morphometric differences between spine dendrites of mice with Fragile X and spine dendrites of normal mice. A set of 286 mice spine dendrites, 220 of which have Fragile X disease is being studied. To date two LDDMM runs comparing each dendrite to two templates have been performed.
  - LDDMM: Implement grid technology. This will allow large anatomical structures to be analyzed using parallel processing.
  - JHU and Johns Hopkins Hospital GCRC are conducting preliminary discussions to establish what GCRC datasets will be made available to BIRN. The most promising datasets are likely to come from the structural and diffusion tensor neuroimaging studies of the auditory cortex. An initial step is to develop acceptable institutional IRB protocols that will result in making these datasets available to BIRN. Then these datasets will be used in shape analysis of structures pertinent to the biological study.

- **Multi-Institutional Research in Analysis of Depression (MIRIAD)**
  As a proof-of-concept study in the application of multi-site mBIRN technologies to retrospective data collections, the MIRIAD effort has shown the feasibility of the effort in generating publishable clinical results while at the same time driving the development of the infrastructure. In the next phases of the mBIRN, we plan to address the key areas where generalization of the processing tools will allow the application of these same tools in other experimental settings sharing broadly similar requirements; initially in the study of Multiple Sclerosis (MS) lesions. Ultimately, relying on the segmentation tools that will operate successfully on legacy data sets will enable a broad selection of potential applications for further quantitative morphometric analysis. The following areas will be emphasized for generalization:

- Data upload: the MIRIAD processing stream currently relies on custom-coded data conversion and data transfer scripts specific to the retrospective data format. We plan to standardize on analysis of DICOM data sets with a simple data description interface, relying on the mBIRN data management tools.
- Selection of processing steps: The MIRIAD analyses were performed by computer scientists who hand-adjusted the parameters of the processing tools to generate the needed accuracy. Newer generations of the processing tools, along with the experience gained from the application of the tools to depression and MS data sets are expected to result in a more broadly applicable set of parameters. For example, we plan to apply the mBIRN white matter atlas work to the retrospective analysis of lesion locations within white matter in an attempt to correlate depression outcomes with proximity of lesions to key signaling pathways (we call this emerging effort the BIRN Effort to Localize Lesions or BELL).
- The cluster computing solution used in MIRIAD was specific to the software infrastructure provided by BIRN-CC on a development cluster installed at SDSC. BIRN-CC is migrating to a more demand-driven method of resource discovery to allocate time on compute resources and we plan to take advantage of this for MIRIAD-like projects going forward.
- Statistical analysis should move increasingly into the BIRN Portal's statistics interface as it develops and integrates advanced hypothesis generation and testing facilities including those being developed as part of the mBIRN machine learning initiatives.

The combination of these developments will lead us toward the vision of distributed groups of imaging researchers collaborating on image analysis projects using only mBIRN infrastructure – that is, where no dedicated hardware or software resources beyond routine scanner equipment are installed locally at the investigators site, and instead are accessed remotely through the BIRN. Even more importantly, this scenario will minimize the amount of computer science expertise required on the part of imaging researchers while still supporting leading edge clinical research.

- **Multi-site Alzheimer's Disease (MAD) project**
  Study Phases and Conference presentation goals: We will begin with a cross-site study of hippocampal volume with cranial vault estimates for proportionalized measures using control participants only, no patients. We expect this study will estimate true site effects and will replicate findings already reported in the literature for single site studies such as normal aging related volume loss, sex effects and interactions, and will examine potential education effects. We are targeting completion of the preliminary analysis to allow an abstract presentation at the Society for Neurosciences meeting in 2005. We will then move forward with patient and control comparisons of hippocampal volume with cranial vault estimates for proportionalized measures, controlling for site effects. We expect to replicate published findings from our groups and others showing greater volume loss in subjects who convert to AD or who are diagnosed with AD. We will examine the relation between volume loss and dementia severity (using MMSE as the critical variable) within impaired groups. We will also examine the relation between volume loss and memory as measured by neuropsychological assessments. These benchmark studies will provide the scientific community can with methods for combining retrospective, legacy imaging data sets to conduct new analyses.

E Publications

Below is a list of accepted and submitted publications in the report period. PDFs of the accepted publications can be found on the Morphometry BIRN wiki pages (http://www.na-mic.org/Wiki/index.php/Mbirn:_Recent_Publications). Abstracts of the submitted papers can be found in section **III Apendix C**.

Manuscripts

- Neu SC, Valentino DJ, Toga AW. *The LONI Debabeler: a mediator for neuroimaging software*. Neuroimage. 2005 Feb 15;24(4):1170-9
- Rex DE, Shattuck DW, Woods RP, Narr KL, Luders E, Rehm K, Stolzner SE, Rottenberg DA, Toga AW. *A meta-algorithm for brain extraction in MRI*. Neuroimage. 2004 Oct;23(2):625-37
- C Fennema-Notestine, IB Ozyurt, CP Clark, S Morris, A Bischoff-Grethe, MW Bondi, TL Jernigan, B Fischl, F Segonne, DW Shattuck, RM Leahy, DE Rex, AW Toga, KH Zou, the Morphometry BIRN and GG Brown.*Quantitative Evaluation of Automated Skull-Stripping Methods Applied to Contemporary and Legacy Images: Effects of Diagnosis, Bias Correction and Slice Selection*. Human Brain Mapping, 2005. (in press)
- B Chen, H Guo, AW Song.*Fast Correction for Direction-Dependent Distortions in Diffusion Tensor Imaging Using Matched Magnetic Field Maps*. (Submitted to NeuroImage)
- JR MacFall, WD Taylor, DE Rex, S Pieper, ME Payne, DR McQuoid, DC Steffens, R Kikinis, AW Toga, RR Krishnan. *Lobar Distribution Of Lesion Volumes In Late-Life Depression: Biomedical Informatics Research Network (BIRN).* (Submitted to Archives of General Psychiatry)
- JA. Turner, P Smyth, JH. Fallon, F Macciardi, JL. Kennedy, SG. Potkin, FIRST BIRN. *Imaging phenotypes and genotypes in schizophrenia*, 2005 (Submitted to Neuroinformatics).

Peer-reviewed Conference Abstracts

- J Jovicich, MF Beg, S Pieper, C Priebe, MM Miller, R Buckner, B Rosen, Morphometry BIRN. *Biomedical Informatics Research Network: Integrating Multi-Site Neuroimaging Data Acquisition, Data Sharing and Brain Morphometric Processing* . The 18th IEEE International Symposium on Computer-Based Medical Systems (IEEE CBMS 2005)
- B. Chen, H. Guo and AW. Song, *Multi-directional distortion correction for DTI*, International Society of Magnetic Resonance in Medicine, Miami May 2005
- J. Jovicich, S. Czanner, D. Greve, J. Pacheco, E Busa, A. van der Kouwe, Morphometry BIRN, B. Fischl., *Test-retest reproducibility assessments for longitudinal studies: quantifying MRI system upgrade effects.* International Society of Magnetic Resonance in Medicine, Miami May 2005

Other Conference Abstracts

- M Faisal Beg, R Buckner, B Fischl, Y Park, E Ceyhan, C Priebe, C Ceritoglu, A Kolasny, T Brown, B Quinn, P Yu, B Gold, J. T Ratnanather, M Miller, BIRN Brain Morphometry. *Pattern classification of hippocampal shape analysis in a study of Alzheimer's Disease*, 2005 Human Brain Mapping Conference.
- X Han, J Jovicich, D Salat, A van der Kouwe, B Dickerson, D Rosas, N Makris, A Dale, B Fischl. *CNR Comparison of three pulse sequences for structural MR Brain Imaging* 2005 Human Brain Mapping Conference
- J Jovicich, S Czanner, B Quinn, J Pacheco, A van der Kouwe, PJ Snyder, M Analoui, M Albert, R Desikan, R Killiany, B Fischl, B Dickerson. *Test-retest reliability assessment for longitudinal MRI studies: An intensity-based comparison of T1-weighted protocols and field strengths* 2005 Human Brain Mapping Conference B Quinn, E Fenstermacher, X Han, J Pacheco, S Czanner, A van der Kouwe, P Maguire, D Raunig, M Albert, N Makris, R Desikan, R Killiany, B Dickerson, B Fischl. *Test-retest reliability assessment for longitudinal MRI studies: A comparison of the effects of different T1-weighted protocols, scanner platforms, and field strengths on semi-automated hippocampal volume measures.* 2005 Human Brain Mapping Conference

III Appendix

A Morphometry BIRN Core Projects proposed in Oct 2004 renewal

Specific Aims

The broadly defined mission of the NIH/NCRR funded Biomedical Informatics Research Network (BIRN- http://www.nbirn.net) project is to develop a scalable network of data acquisition techniques, databases and computational resources that can support the biomedical research enterprise. The Morphometry BIRN (mBIRN) test bed consortium project has initiated work to remove obstacles to the use of anatomically based biomedical imaging data as clinically relevant, quantitative biomarkers that are site and hardware independent. The mBIRN project has initiated the development and validation of image acquisition tools that are imaging platform independent, begun development of an integrated suite of image analysis tools from multiple BIRN partners to quantify these data in a variety of ways, and started to deploy robust data base structures that can store, retrieve, query and protect these complex imaging and associated metadata. These tools form the foundation of the mBIRN consortium, and are additionally being used as the anatomical basis set for the Functional Imaging Research Schizophrenia Test bed BIRN (FIRST BIRN) project.

In this competing renewal application, we propose three broad areas of work (Projects 1-3) to refine and expand upon our initial success: Project 1) optimization and validation of multi-site structural MRI acquisition and calibration methods, with extension to include additional imaging contrasts (T2 and DTI); Project 2) continued development of morphometric analysis, visualization, and interpretation tools; Project 3) continue the development of a neuroinformatics infrastructure that will deliver efficient data management, dynamic access, and application-based querying to neuroimaging data and the associated neuropsychiatric, behavioral and neurogenetic data. In the Clinical Collaboration section we propose our methods to propagate widespread application and use of the mBIRN infrastructure in support of an expanding set of clinical domains, using a phased approach. Finally, our Administrative Core section reviews our internal and external structures for coordinating the activities across our disparate sites, and discusses our plans to assure widespread dissemination of the mBIRN toolbox.

Specifically, we propose the following Projects, with their associated specific aims:

Project 1 Standardize and calibrate the acquisition of high-resolution structural MRI data to facilitate precise, quantitative, platform independent, multi-site evaluation of normal and pathological structural imaging data at multiple field strengths.

- **1.1** Develop methods to improve structural T_1- and FSE-based PD, T_2-weighted, and FLAIR weighted MRI acquisition protocols that maximize image quality, improve sensitivity, reduce noise and enable quantitative analysis of healthy and diseased tissue across sites and instruments.
- **1.2** Extend these methods to the acquisition of diffusion sensitive imaging, to improve diffusion MRI protocols and correction methods that minimize variability across sites while optimizing image quality and sensitivity for reconstructing fiber tracts and detecting abnormalities.

Project 2 Continue to develop, integrate and deploy a suite of freely available software to enable scientific investigation of the morphological bases of function and dysfunction through increasingly sophisticated image analysis on increasingly large subject populations acquired at multiple research sites.

- **2.1** Adapt and apply automated and semi-automated tools to segment subcortical structures, delineate the cortex, and parcellate cortical functional and anatomical regions from a range of input image protocols by drawing on expertise and existing software of the participating institutions.
- **2.2** Adapt and apply shape-based morphometric tools to investigate clinical and control populations: continue to develop interoperability between segmentation and shape analysis tools through standardized data representation.

2.3 Integrate Diffusion Tensor Imaging (DTI), anisotropy measurements, white matter (WM) atlases, and automated tractography techniques into the BIRN morphometry analysis infrastructure.
2.4 Provide an integrated visualization tool to support detailed investigation of morphometry and other data types.
2.5 Develop a visualization-based query tool to facilitate knowledge discovery and development of scientific explanations.
2.6 Adapt and apply machine-learning techniques to identify statistically related subpopulations of study subjects based on biomedical images.

Project 3 Create an infrastructure that will ensure efficient data management, reliable processing and dynamic access to imaging, behavioral, clinical and genetic data.
3.1 Continue to develop and deploy an extensible database, that can be adapted to fulfill a local site's needs and that interoperates with the federated BIRN database infrastructure
3.2 Extend the BIRN infrastructure based on the capabilities and needs of the mBIRN collaborators to incorporate T2, FLAIR, and diffusion image data and genetic information.
3.3 Develop, test, and validate automated graphical protocols for data integration, pre- and post-processing and display.

Clinical Collaboration The goal is to propagate widespread application and use of the mBIRN infrastructure in an expanding set of clinical domains, using a phased approach. During the first phase of the renewal period collaborative projects will address questions directly in line with the broad clinical directions of the original mBIRN application – quantitative structural neuroimaging investigation of dementia and depression. This will first include sites with investigators already participating in mBIRN, but will subsequently be extended to include a broad array of sites through our collaboration with the new NIA Alzheimer's Disease Neuroimaging Initiative (ADNI). In the second phase this effort will be expanded to include new areas of clinical investigation, outside of AD and depression, that require quantitative structural neuroimaging. In the final phase we will identify new collaborators and implement new methods to support quantitative structural imaging. Throughout, we propose to disseminate the tools and research resources of mBIRN to the broader scientific community through collaborations the NCRR funded General Clinical Research Centers (GCRCs) both locally and nationally, and through interactions with other national organizations, including the NIFTI program and the Radiological Society of North America, interested in utilizing BIRN resources to aid in studies within and outside the brain.

Administrative Core The mBIRN Administrative Core will be responsible for addressing the many and complex logistical, administrative, financial and ethical issues associated with the project and its new mandates. The proposed Administrative Core supports the efforts of Dr. Bruce Rosen, the overall mBIRN project PI, Dr. Jorge Jovicich, the mBIRN Project Manager, Monica Langone, who will manage the financial responsibilities, and Phyllis Somers, the clinical coordinator who will be responsible for administration of the human studies aspects of the project. The Core will provide support for the many working groups and both internal and external committees required to facilitate and coordinate the broad list of activities of this large and complex project.

Computational "Distributed Core" A distributed group of computer scientists and database experts will be assembled in a "virtual" manner, and includes investigators from the BIRN Coordinating Center (BIRN CC), and a group of investigators from MIT and the Partners Health Care System who are supported specifically by the mBIRN test bed, and who have expertise specifically required by the mBIRN Projects above.

B Morphometry BIRN participants and roles

Morphometry BIRN Personnel Budget	**Brain Morphometry BIRN Sites and Roles**		
	Funded Personnel	**FTE**	**Roles**
Administration Core			
MGH	B. Rosen	15%	Principal Investigator
	J. Jovicich	100%	Project Manager
	M. Langone	50%	Administrative Assistant
	P. Somers	30%	Administrative Assistant
Computation Core			
MGH	S. Murphy	10%	Co-Investigator (Workflows)
	M. Mendis	100%	Database Engineer (Workflows)
MGH Site	B. Rosen	10%	Principal Investigator
	D. Kennedy	20%	Site PI (Data Management Leader)
	R. Gollub	25%	Scientific Director
	B. Fischl	5%	Co-Investigator (MRI Calibration, Freesurfer optimization)
	P. Raines	25%	Network Engineer
	S. Czanner	100%	Software Engineer (MRI Calibration)
	K. Teich	100%	Software Engineer (Freesurfer optimization)
	H. Schmidt	100%	Database Engineer (Data Management)
	E. Busa	100%	Research Assistant (Freesurfer processing, quality assurance)
	A. vd Kouwe	5%	MR Sequence Programmer (MRI Calibration)
Total MGH FTE		7.95	
BWH Site	R. Kikinis	5%	Site PI
	S. Pieper	20%	Co-Investigator (Analysis, Visualization & Interpretation Core leader)
	N. Aucoin	75%	Software Engineer (Data Provenance)
	T. Zlatnov	15%	Network Engineer
	W. Wells	5%	Co-Investigator (Protocol neutral segmentation developments)
	S. Warfield	5%	Co-Investigator (Protocol neutral segmentation optimization on MS data)
	CF Westin	5%	Co-Investigator (Development and extensions of diffusion MRI modules in Slicer)
	K. Zou	5%	Co-Investigator (statistical analysis support in multi-site MRI calibration)
	R. Estepar	75%	Postdoc (3D Slicer support for DTI applications)
Total BWH FTE		2.10	
MIT Site	E. Grimson	5%	Site PI
	P. Golland	5%	Co-Investigator (Machine Learning to analyze imaging metadata)
	T. Jaakkola	5%	Co-Investigator (Machine Learning to identify statistically related subpopulations)
	D. Karger	5%	Co-Investigator (Semantic web tools for database management and retrieval tools)
	S. Madden	5%	Co-Investigator (Database tools for semantic web applications)
	Karun Bakshi	100%	Research Assistant (Haystack project, semantic data mining)
	Mahnaz Maddah	100%	Research Assistant (Machine Learning in image context, classification, clustering)
Total MIT FTE		2.25	
WashU Site	R. Buckner	15%	Site PI
	D. Marcus	80%	Co-Investigator (Data Management Tools)
	S. Goldkind	40%	Computer Systems Manager
	M. Ramaratnam	100%	Software Engineer (Data Management Tools)
	TBD	50%	Software Engineer (Data Management Tools, dissemination to GCRC)
Total WashU FTE		2.60	

Morphometry BIRN Personnel Budget	Brain Morphometry BIRN Sites and Roles		
	Personnel	**FTE**	**Roles**
JHU Site	M. Miller	0%	Site PI
	A. Kolasny	40%	Network Engineer (LDDMM/SRB/Teragrid developments)
	T. Brown	100%	Database Engineer (LDDMM/SRB/Teragrid developments)
	S. Mori	2%	Co-Investigator (co-lead multisite diffusion MRI calibration)
	X. Xu	100%	Research Technician (MRI data acquisition and data management)
	K. Hua	20%	Research data coordinator (MRI data analysis)
	J. Morra	50%	Research Technician (extraction of Brainworks modules for applications in SASHA pipeline)
Total JHU FTE		2.75	
Duke Site	R. Krishnan	5%	Site PI
	J. MacFall	7.7%	Co-Investigator (lead data acquisition, analysis, calibration for lesion detection work)
	A. Song	5%	Co-Investigator (co-lead multisite diffusion MRI calibration)
	F. Favaroni	40%	Analyst Programmer (local BIRN rack support)
	S. Gadde	66%	Analyst Programmer (computer support for DTI)
	B. Boyd	100%	Computer Programmer (software developer, data management, local GCRC liaison)
	M. Payne	25%	Research Associate (IRB, assist/supervise lesion detection work)
	TBD	100%	Postdoc Trainee (support for lesion detection analysis and DTI calibration)
	S. Rusincovitch	100%	Data Technician
Total Duke FTE		4.487	
UCSD Site	A. Dale	20%	Site PI
	L. Frank	10%	Co-Investigator (support for multisite diffusion MRI calibration)
	W. Kremen	20%	Co-Investigator
	C. Notestine	50%	Co-Investigator (Ontology work, Multi-site AD application test)
	B. Ozyurt	50%	Database Engineer (HID developments)
	R. Notestine	50%	Software Engineer (support for MRI calibration)
	M. Perry	100%	Research Assistant (support MRI calibration acquisition and analyses)
	TBD	100%	System Administrator
	K. Lu	35%	MR Sequence Programmer (support for multisite MRI calibration)
Total UCSD FTE		4.55	
UCLA Site	A. Toga	3%	Site PI
	K. Crawford	30%	Database Manager (LONI database configuration, interface with users)
	I. Dos Santos	75%	Database Assistant (LONI database develoments)
	R. Magsipoc	30%	Network Administrator
	S. Neu	40%	Knowledge Expert (LONI database develoments)
	R. Nor	70%	Computer Programmer (LONI database statistical methods development)
Total UCLA FTE		2.48	
UCI Site	S. Potkin	10%	Site PI
	P. Smyth	10%	Computer Scientist
	J. Fallon	15%	Co-Investigator (White Matter Atlas generation and neuroscientist-friendly diffusion tools)
	D. Keator	40%	Software Engineer
	D. Wei	25%	Database Engineer
	S. Chen	32%	Network Engineer
	HJ Lee	100%	Research Assistant
Total UCI FTE		2.32	

C Abstracts of submitted papers

- B Chen, H Guo, AW Song.*Fast Correction for Direction-Dependent Distortions in Diffusion Tensor Imaging Using Matched Magnetic Field Maps*. (Submitted to NeuroImage)

  Abstract: *Diffusion tensor imaging (DTI) has seen increased usage in clinical and basic science research in the past decade. By assessing the water diffusion anisotropy within biological tissues, e.g. brain, researchers can infer different fiber structures important for neural pathways. A typical DTI dataset contains at least one base image and six diffusion weighted images along non-collinear encoding directions. The resultant images can then be combined to derive the three principle axes of the diffusion tensor and their respective cross terms, which can in turn be used to compute fraction anisotropy (FA) maps, apparent diffusion coefficient (ADC) maps, and to construct axonal fibers. The above operations all assume that DTI images along different diffusion-weighting directions for the same brain register to each other without spatial distortions. This assumption is generally false, as the large diffusion-weighting gradients would usually induce eddy currents to generate diffusion weighing direction dependent field gradients, leading to mis-registration within the DTI dataset. Traditional methods for correcting magnetic field induced distortions do not usually take into account these direction-dependent eddy currents unique for DTI, and they are usually time consuming because multiple phase images need to be acquired. In this report, we describe our theory and implementation of a fast, efficient and effective method to correct for the main field and eddy current-induced direction-dependent distortions for DTI images under a unified framework to facilitate the daily practice of DTI acquisitions.*

- JR MacFall, WD Taylor, DE Rex, S Pieper, ME Payne, DR McQuoid, DC Steffens, R Kikinis, AW Toga, RR Krishnan. *Lobar Distribution Of Lesion Volumes In Late-Life Depression: Biomedical Informatics Research Network (BIRN).* (Submitted to Archives of General Psychiatry)

  Abstract: *Context: White matter hyperintense lesions on T2-weighted MR images are associated with late-life depression. Little work has been done examining differences in lesion location between elderly individuals with and without depression. Objective: To examine lobar differences in white matter lesion volumes derived from brain MR imaging. Design: Case-control study. Participants: 49 subjects with a DSM-IV diagnosis of Major Depression and 50 comparison subjects without depression. All participants were age 60 years or older. Outcome Measures: White matter lesion volumes were measured in each hemisphere using a semi-automated segmentation process and localized to lobar regions using a lobar atlas created for this sample using the imaging tools provided by the Biomedical Informatics Research Network (BIRN). The lobar lesion volumes were compared against depression status. Results: After controlling for age and hypertension, subjects with depression exhibited significantly greater total white matter lesion volume in both hemispheres and in both frontal lobes than did control subjects. Although a similar trend was observed in the parietal lobes, the difference did not reach a level of statistical significance. Models of the temporal and occipital lobes were not statistically significant. Conclusions: Older individuals with depression have greater white matter disease than healthy controls, predominantly in the frontal lobes. These changes are thought to disrupt neural circuits involved in mood regulation thus increasing the risk of developing depression.*