National Alliance for Medical Image Computing
Annual Research Progress Report-2006

Contents

National Alliance for Medical Image Computing Second Annual Research Progress Report 2006

Introduction

The National Alliance for Medical Imaging Computing (NA-MIC) is now in its second year. The Center is comprised of a multi-institutional, interdisciplinary team of computer scientists, software engineers, and medical investigators who have joined forces to develop and apply computational tools for the analysis and visualization of medical imaging data. A further purpose of the Center is to provide infrastructure and environmental support for the development of computational algorithms and open source technologies, and to oversee the training and dissemination of these tools to the medical research community. The driving biological problems (DBPs) come from schizophrenia, although the methods and tools developed are clearly applicable to many other diseases. In the first year of this endeavor, our main focus was to build alliances among the many cores and to increase awareness of the kinds of tools needed for specific imaging applications. Our first Annual Report and All-Hands meeting reflected this emphasis on cores, which was necessary to bring together members of an interdisciplinary team with diverse expertise and interests.

The emphasis in year two has shifted from the integration of cores to the identification of themes that cut across cores, driven by the requirements of the DBPs. The four emerging themes are Diffusion Image Analysis, Structural Analysis, Functional MRI Analysis, and Integration of newly developed tools into the NA-MIC Kit. Each of these lines of inquiry represents a collaboration of effort by the computer scientists, clinical core counterparts, and engineering partners of the seven NA-MIC cores. Our progress can be measured by the numerous publications authored and presented by NA-MIC investigators over the past year (Appendix A).

The report begins with a summary of current progress in the context of our Four Main Themes: Diffusion Image Analysis, Structural Analysis, Functional MRI Analysis, and the NA-MIC Kit. Each of these sections begins with an overview of the theme, provides a progress update and list of key investigators, and concludes with a set of web links to individual projects in that theme. The report then highlights three important accomplishments of the second year: the NA-MIC Software Process, a clinical application of Diffusion Tensor Imaging, and our Outreach Efforts. We review the impact and value of our work to the biocomputing community at three different levels: within the Center, within the NIH-funded research community, and at the national and international level. Finally, we provide a timeline of Center activities, which is based on the specific aims of our original proposal, and the report of our External Advisory Board. A complete list of current publications (Appendix A) and an organizational chart of the seven NA-MIC cores (Appendix B) are included for reference.

Four Main Themes

Theme 1: DIFFUSION IMAGE ANALYSIS

Over the past year, we have developed tools relevant to diffusion tensor estimation, fiber tractography, and geometric and statistical diffusion tensor analysis. These tools have already been integrated into diffusion-dedicated software (i.e., Fiber viewer-UNC, Slicer -Harvard-BWH/MIT) and are currently being used in multiple clinical projects involving several psychiatric populations (schizophrenia, schizotypal personality disorder, and bipolar disorder), in addition to normal controls. Below we provide a more detailed review of our progress in the area of diffusion image analysis.

Research Progress

Fiber Tract Extraction and Analysis

- Fiber tractography has been implemented in both "Fiber viewer" and "Slicer" packages. New developments have been made in terms of fiber tractography generation (using anisotropic energy function), post-processing including fiber clustering (i.e., using shape similarity-based fiber separation/grouping), and statistical fiber comparison. The latter technique is especially important for studying population differences and has already been used in clinical investigations of schizophrenia.

- Fiber tractography and geometric estimation of diffusion have been integrated, which makes feasible the estimation of diffusion properties along fiber tracts. These procedures have already been implemented in clinical studies. For example, fiber tractography is being applied to manually drawn cingulum bundle regions of interest to generate the entire cingulum bundle fiber tract. Next, fractional anisotropy and other diffusion anisotropy metrices, such as mode, linear, planar, and spherical diffusion index, as well as geodesic diffusion, will be calculated along the fiber tracts and compared between populations.

- We are developing a method for elastic registration of diffusion tensor images that would permit direct comparison of diffusion tensor properties between groups, as well as the generation of templates and white matter fiber atlases. This method requires image-matching metrics, interpolation of tensor images, and tensor image transformations. A great deal of progress has been made in each of these representative areas.

- We have also developed a method for integrating registration and shape-based tract grouping into population clustering, where brain fibers are labeled into anatomically relevant fiber tracts based on their shape and anatomic location across multiple subjects. This method is currently being applied to the NA-MIC schizophrenia data.

Fractional Anisotropy Analysis

We have developed tools that permit diffusion anisotropy estimation comparison along the entire fiber bundles generated by means of fiber tractography. In addition to popular diffusion indices, such as fractional anisotropy, there are new diffusion measures that more precisely describe diffusion properties, such as mode, geodesic diffusion, linear, planar, and spherical diffusion indices. These have been introduced and are being tested on the NA-MIC data set and applied to other clinical projects described below:

- Connections between frontal and temporal lobes including the uncinate fasciculus, fornix, and cingulum bundle are being investigated in schizophrenia, schizotypal personality disorder, and bipolar disorder by applying already existing (fractional anisotropy, relative anisotropy, trace) and new (mode, geodesic diffusion) diffusion metrices to the regions of interest available through the NA-MIC data set.

- The same diffusion indices are also being estimated along the paths generated with fiber tractography.

- Interhemispheric connections that include the anterior commissure and corpus callosum are being investigated by estimating the anisotropy indices listed above along the fiber paths generated with fiber tractography. In addition, fiber clustering, which permits differentiation of fiber bundles that interconnect with different anatomic subregions of the brain, is being applied to interhemispheric connections.

Integration of fMRI and DTI Path-of-Interest (POI) Analysis

We are actively working on ITK tool to register functional MRI (fMRI) and diffusion tensor imaging (DTI) data that would result in the further integration of information from different imaging modalities. Additionally, we are working on a newly developed optimal path analysis (Harvard-MGH), which is being tested at both Dartmouth and Harvard-BWH. This path analysis is meant to integrate diffusion and functional information, as well as to generate optimal anatomic connections between brain regions activated during fMRI experiments.

DTI Validation

Understanding the biological meaning of measures obtained from DTI has been one of our principal objectives. Thus, various projects have been undertaken this year to validate the precision of different algorithms generating fiber tracts ("DTI studio," "Slicer," "Fiber tracker"), by applying them to different DTI data sets (John Hopkins, Dartmouth, Harvard-BWH) and comparing the results against each other, as well as against postmortem investigations and anatomic atlases. In addition, the specificity of diffusion measures is being validated by finding correlates among neuropsychological and clinical measures.

Algorithms and Software Infrastructure
Over the past year, two complete, publicly available tools critical for diffusion tensor imaging and data analysis have been released: Slicer DTI module, and Fiber viewer.

- ***Slicer DTI module*** developed at Harvard-MGH and MIT includes a tensor estimation algorithm, as well as newly enhanced algorithms for fiber tractography. Among these are region-of-interest (ROI) guided fiber extraction and shape-based clustering. Of further note, Slicer can now generate maps of various diffusion indices, including mode, linear, planar, and spherical diffusion.

- ***''Fiber tracker" and "fiber viewer,"*** both developed at UNC, are stand-alone diffusion tools capable of tensor estimation, fiber tractography, and geometric and statistical data analysis. The statistical comparison mode is enhanced by the plane-cutting utility, and diffusion indices can be generated and compared along the fiber tract. In addition, several modes of fiber clustering and diffusion tensor image filtering developed at the University of Utah are all part of these new tools.

Additional infrastructural work has been undertaken (Harvard-MGH, Kitware, Dartmouth) in the utilization of non-rigid EPI registration techniques to better compensate for otherwise uncorrected eddy current artifacts and to provide a better framework for intersubject registration in support of group DTI analysis methods. This task involves optimization of registration parameters, as well as validation testing in comparison to linear methods.

Key Investigators
- **Harvard-BWH: (PNL)** Martha Shenton, Marek Kubicki, Marc Niethammer, Sylvain Bouix, Mark Dreusicke, Katarina Quintus, Doug Markant **(SPL)** Carl-Fredrik Westin, Raul San Jose, Gordon Kindlmann
- **Harvard-MGH:** Dave Tuch, Denis Jen, Josh Snyder
- **MIT:** Lauren O'Donnell
- **UCI:** James Fallon, Martina Panzenboeck
- **UNC:** Guido Gerig, Isabelle Corouge, Casey Goodlett, Martin Styner
- **Utah:** Tom Fletcher, Ross Whitaker, Saurav Basu
- **GATech:** Eric Pichon, John Melonakos, Xavier LeFaucheur, Allen Tannenbaum
- **Dartmouth:** John West, Andrew Saykin, Laura Flashman, Paul Wang, Heather Pixley, Robert Roth
- **Isomics:** Steve Pieper

Link to Additional Information

For details on individual projects in this theme, please see [[NA-MIC_Internal_Collaborative_Projects#Diffusion Image Analysis|NA-MIC Projects on Diffusion Image Analysis]].

Theme 2: STRUCTURAL ANALYSIS

Research Progress
Structural image analysis is concerned with the morphology of anatomic structures, which includes the identification and characterization of volume and shape. This analysis consists of image filtering, tissue segmentation, the anatomically true subdivision of large structures into relevant substructures, and the extraction of features to be used for population-based statistical analysis. Of note, linear and nonlinear volumetric registration tools have multiple uses, i.e., mapping individual image data sets into an anatomic reference database, fusing data by combining multiple modalities, and linking the individual anatomy to a statistical prior (atlas). These tools are also critically important to structural image analysis. NA-MIC is developing a new set of tools driven by the needs of its clinical partners (Core DBPs), using the existing image databases for testing and validation. The development of methods and tools for structural image analysis is a collaborative effort between the computer science partners in Core 1, clinical Core 3 counterparts, and engineering Core 2 partners. This collaborative approach ensures the development of state-of-the-art methods that are driven by the requirements of clinical imaging research and implemented with industry-standard programming style and design.

Image Segmentation

• **Utah** Efforts here have involved the development of multi-spectral MRI tissue classification with a novel spatial filtering scheme using Markov random fields. In addition, a comparison of the new segmentation method to expectation-maximization (EM-) segmentation (Leemput et al.) has been completed based on simulated data (MNI) with varying levels of noise.

• **GATech** Efforts here have involved the development of rule-based semi-automatic segmentation tools, which include a "thumb extractor" using energy-based minimization for efficiency and a Bayesian tissue classifier. Both tools have been combined with rules developed by Jim Fallon (UCI) and Jim Levitt (Harvard-BWH) and integrated into a Graphical User Interface (GUI) to efficiently segment the dorsolateral and dorsomedial prefrontal cortex (DLPFC and DMPFC), putamen, and striatum. Rule-based striatum segmentation has also been integrated into Slicer and thus is already part of the NA-MIC toolkit.

• **GATech** One area of focus has been on statistical partial differential equation (PDE) methods: Statistical measures were added into the PDE method (curvature driven flow), which allows incorporation of global image information into a locally defined PDE framework.

• **MIT** Shape-driven segmentation using an EM framework has been used for statistical segmentation. The tool uses registration of atlas information (shape prior) to

guide subtle segmentation and incorporates additional statistical shape information to refine the segmentation of substructures. Preliminary validation has been completed on 22 scans where expert segmentations are available. The development of atlas priors and statistical shape models has also been conducted in close collaboration with the clinical partner group of M. Shenton, Harvard, Psychiatric Neuroimaging Laboratory (PNL). The segmentation system is currently integrated into the Slicer platform.

• **Dartmouth** Volumes of medial temporal lobe structures in patients with schizophrenia, including the hippocampus, amygdala, and entorhinal cortex, have been measured with Slicer using manual segmentation.

Image Registration

• **GATech** Registration of pairs of image data sets has been done via registration of segmented surfaces. Using sulci as landmarks, surfaces are flattened to an annulus and mass-preserving mapping is used to register the two annuli.

• **Isomics** Slicer Registration Framework (Registration Tools): The registration framework is designed to support translation, rigid, affine, and deformable forms of registration between volumetric image data in Slicer. These tools will form a most crucial component of the NA-MIC toolkit, since linear and nonlinear image registration is a key component for segmentation, morphometric analysis, and data fusion.

Morphometric Measurements and Shape Analysis

• **UNC** A toolkit for population-based statistical shape analysis has been implemented, which runs as a dataflow pipeline. ITK modules include surface parametrization [(spherical, harmonics, and point distribution models (PDMs)], surface correspondence, shape alignment, statistical analysis with correction for multiple comparison, and visualization of complex statistics for verification and interpretation. Application to Harvard VA SPD clinical study of caudates (20 SZ and 20 CNTL), second BWH SPD caudate study, and Dartmouth hippocampus study (20 SZ and 20 CNTL) in close collaboration with Core 3 partners.

• **UNC** The LONI shape pipeline prototype for automatic population-based shape analysis has been implemented in collaboration with UCLA (LONI pipeline) and with GE (Dart 2 based data storage).

• **GATech** Localized shape analysis using spherical wavelet basis functions has been used to encode local shape in space at different scales. Application to the BWH caudate data set has been done with comparison of wavelet prior estimation with principal component analysis (PCA) estimation.

• **MIT** Shape modeling of anatomical structures of interest has been conducted to be used as a shape prior for segmentation. Shapes are coded via distance transforms and represented as mean shapes plus major eigenmodes of deformations. The result is a multi-object hierarchical representation of brain structures.
• **Utah:** Automated shape model construction: A tool to automatically construct shape models from an input of several binary segmentations. This method finds boundary correspondences by creating the most efficient probability distribution for the population of input shapes, and can be used for statistical group comparison. Hippocampal segmentations from Harvard are used as a driving clinical application.

Algorithms and Software Infrastructure
Most of the new tools listed above are either already integrated into Slicer or are available as ITK modules of the NA-MIC toolkit. Complex sequences of tools such as rule-based segmentations, shape-driven EM segmentation, or population-based shape analysis are developed as sets of ITK modules, which, in turn, are integrated into Slicer, into a separate GUI for testing and validation, or combined to automatic pipelines via the LONI pipeline architecture.

Key Investigators
• **MIT** Kilian Pohl, Eric Grimson
• **UNC** Martin Styner, Ipek Oguz, Guido Gerig
• **Utah** Ross Whitaker, Suyash Awate, Tolga Tasdizen, Tom Fletcher, Joshua Cates, Miriah Meyer
• **GaTech** Allen Tannenbaum, John Melonakos, Tauseef ur Rehman, Shawn Lankton, Ramsey Al-Hakim, Eric Pichon, Delphine Nain, Oleg Michailovich, Yogesh Rathi, James Malcolm
• **GE, Kitware, Isomics** Steve Pieper, Bill Lorensen, Luis Ibanez, Karthik Krishnan, Michael J. Pan, Jagadeeswaran Rajendiran, Jim Miller, Karthik Krishnan, Luis Ibanez
• **Harvard-BWH (PNL)** Sylvain Bouix, Motoaki Nakamura, Min-Seong Koo, Martha Shenton, Marc Niethammer, Jim Levitt **(SPL)** Sandy Wells
• **Dartmouth** Andrew Saykin
• **UCI** James Fallon

Link to Additional Information

For details of each of the projects in this theme, please see [[NA-MIC_Internal_Collaborative_Projects#Structural Image Analysis|NA-MIC Projects on Structural Image Analysis]].

Theme 3: FUNCTIONAL MRI ANALYSIS

Research Progress
A fundamental challenge for the DBPs is defining the circuitry that subserves the major cognitive operations that are dysfunctional in schizophrenia and other neuropsychiatric disorders. Structural MRI can define the location, volume, and shape of key nodes in networks. fMRI defines activation foci that an individual engages while performing a cognitive task. DTI can define the anatomic tracts that constitute the circuitry of interest. Methods are needed for data integration, visualization, and quantitiative measurement across these modalities.

NA-MIC teams have made progress in several key areas related to fMRI during the prior funding period including fMRI software implementation, development of novel analytic methods relating functional, structural, and diffusion brain imaging data, and preliminary applications in several collaborative projects.

Algorithms and Software Development

fMRI Statistics Software Infrastructure The GE team is working to provide ITK and Slicer-based tools for processing fMRI data. Currently, the scope of this effort focuses on the data processing that occurs after the alignment of the time sequence acquisition. As such, the effort is centered on the statistical analysis of fMRI and includes infrastructure for data representation, massively univariate processing, hypothesis testing, and segmentation.

Implementation of fMRI analysis software in Slicer 2 This module has been released in Slicer 2.6. Key features include loading of pre-processed fMRIData, specification of the stimulus schedule for blocked, event-related and mixed designs, signal modeling, contrast definition, and general linear mode (GLM) based analysis of results. Output includes statistics on activation-based regions of interest (ROI) and timecourse plotting on individual voxels and on ROIs. In Slicer's visualization environment, statistical parametric maps of brain activation can be superimposed on high resolution anatomic scans of the same subject, and these data can also be combined with DTI and other data on the same subject. The modular design permits extension to alternate algorithms for activation detection. An in depth tutorial for using this module is being refined and will be tested in our local community. Subsequently, it will be made available to the broader user community. Support for Ising Priors is currently being added to the module.

Spatial Regularization for fMRI Detection An important NA-MIC theme is the integration of structural and functional imaging data to enhance the information yield of each method. We recognized that detection of brain activation in fMRI studies could be enhanced by incorporating spatial priors. A team from MIT (Polina Golland, Wanmei Ou) and Harvard-BWH (Steve Pieper, Sandy Wells, Wendy Plesniak, Carsten Richter) developed a method that employs Markov Random Fields

(MRF) as spatial smoothing priors to address the low signal-to-noise ratio of BOLD fMRI signals. This approach, developed by NA-MIC, extends the MRF prior to include anatomic information. The anatomic prior, in the form of a segmented MRI scan, biases the activation detection towards the gray matter and inhibits smoothing of the activation maps across tissue boundaries. This has the potential to significantly increase statistical power in fMRI experiments. We have validated the method on a set of fMRI scans and are currently working on implementation of the detection algorithm in Slicer. We also plan to release the code into the ITK library to make the method available to a broader community.

Path of interest (POI) analysis for integrating fMRI and DTI To test the study hypotheses regarding abnormal cognitive circuitries, we identified the need for a tool to find optimal and alternative paths between regions of interest in a tensor image. A prototype version of the POI tool was developed by a team from Harvard-MGH (Josh Snyder, David Tuch) and Dartmouth (Andrew Saykin, John West) with DTI coordinate system support from Harvard-BWH (Gordon Kindlmann, Raul San Jose, Steve Pieper). The POI tool accepts fMRI activation foci or structural ROIs as input to drive the identification of POIs. The output is eventually to include probability density images, path statistics, and extracted quantitiative information regarding identified paths. Output can now be visualized in 3D Slicer and future plans include incorporating the POI algorithms into the Slicer DTI analysis module and ROI drawing tools. The prototype POI tool was tested on a 1.5T 12 diffusion direction DTI data set from Dartmouth. We are now planning to test this tool on new 32 diffusion direction 3.0T data from Dartmouth.

Conformal Flattening for fMRI Visualization This project is directed towards development of new flattening methods for better visualizing neural activity from fMRI scans. Conformal mappings are used to map the cortical surface onto a sphere in an angle preserving manner. To date, the team from Georgia Tech and MGH-Harvard has developed code for conformal flattening that has been incorporated into Slicer.

Applications to Functional Brain Activation in Schizophrenia and Related Conditions

Driving Biological Problems

The scientific agenda of Core 3 addresses the abnormalities of regions, systems, and circuitry that underlie higher cognitive deficits in schizophrenia. These DBPs require an integrated advanced image analysis toolkit that can incorporate and relate cortical and subcortical ROI analysis, diffusion tensor maps of anatomic connectivity, as well as fMRI maps of brain activation patterns. Additional targeted functionality includes the ability to register and relate high dimensional structural, functional, and diffusion data sets to individual differences in symptomatology and variation in candidate gene profiles. Core 3.1 focuses on brain connectivity. Specific Aims 1-3 address frontal-temporal connections in schizophrenia, with target pathways including the uncinate fasciculus (Aim 1), cingulate fasciculus (Aim 2), and arcuate fasciculus (Aim 3). Aim

4 is directed toward left and right hemispheric connectivity (corpus callosum) and Aim 5 is to investigate cortical-subcortical circuitry (internal capsule, anterior limb). For each pathway, the emphasis is on abnormalities in cognitive function, related brain activity patterns detected by fMRI, as well as the relationship to clinical symptomatology. Core 3.2 also addresses abnormalities of brain circuitry in schizophrenia using multiple imaging modalities. In addition, Core 3.2 has a special emphasis on genetic variation as an explanatory factor. Aim 1 focuses on the contribution of dysfunction in DPFC and connected forebrain structures to schizophrenic subtypes. Aim 2 addresses the level of organization at which the circuitry produces different clinical syndromes. Aim 3 is to assess the influence of normal genetic allelic variation on the structural and functional changes investigated in Aims 1 and 2.

Neural Substrates of Impaired Memory Systems in Schizophrenia Prior research has demonstrated deficits in multiple memory systems in patients with schizophrenia. These systems include working memory, episodic memory, and semantic memory. Working memory refers to temporary "on-line" storage of small amounts of information used during active task performance and problem solving. Episodic memory is the ability to learn and retain new context-dependent information. Semantic memory includes knowledge of facts and concepts that have become independent of any specific learning context. In the past, clinical and experimental neuropsychologic tests of these memory systems have been used to assess memory performance but more recently memory systems have been assessed during functional brain imaging with fMRI or alternative techniques. Few studies have systematically sampled different memory systems during fMRI and related the results to brain structure and connectivity. Three ongoing NA-MIC subprojects by the Dartmouth and Harvard-BWH teams are addressing this need. The needs of these subprojects are stimulating novel technical approaches to relate fMRI, ROI, and DTI data sets and making use of prototype NA-MIC tools as they emerge to accomplish project goals. In each project, preliminary analyses are being completed that examine fMRI activation patterns and assess connectivity between regional activation sites, both in terms of functional relationships and white matter pathways.

Working Memory in Schizophrenia and Bipolar Disorder: Parametric Analyses This project assesses working memory using an auditory verbal version of the n-back task paradigm. Three conditions are presented in blocks in counterbalanced order with increasing working memory load demands (0-, 1-, 2- and 3-back). To date, 16 patients with schizophrenia, 10 patients with bipolar disorder, and 13 healthy controls have been studied.

Brain Activation during Continuous Verbal Encoding and Recognition in Schizophrenia This project employs an event-related auditory verbal episodic memory probe targeting medial temporal and DLPFC circuitry. The task uses a continuous performance format where concrete nouns are presented initially as new items. Words are then repeated after short or long intervals and the participant is required to make a new/old distinction. This design permits analysis of both encoding and recognition

processes. To date, data have been collected on 8 patients with schizophrenia and 5 healthy controls.

Frontal-Temporal Connectivity in Schizophrenia during Semantic Memory In this project, an event-related auditory semantic memory task is administered. Participants are presented with a semantic category and required to decide whether a subsequent word is a member of the category (e.g., vehicle-bus). To control for phonological processing, other items require a match-mismatch decision between pseudo-words constructed from reordered semantic items (e.g., yodb-rea). To date, 6 patients with schizophrenia and 3 healthy controls have been studied with this task.

Imaging Phenotypes in Schizophrenics and Controls Functional connectivity of the DLPFC by genotype was investigated using partial least squares (PLS) correlation analysis. PLS is a multivariate analytical technique used to summarize large neuroimaging data sets in such a way as to correlate patterns of activation with a variable(s) of interest (i.e., DLPFC activity). In the most recent analysis, the DRD1 genotype was used as a grouping variable. DLPFC activity and working memory accuracy were simultaneously entered as variables of interest. The AA and AG groups showed different primary patterns. Since the two groups did not differ in average performance, this method reveals differences by genotype in covariance across the brain, i.e., differences in connectivity or circuitry, in performing the task. The AA group demonstrated increased "efficiency", e.g., a negative correlation between DLPFC activations and accuracies in both memory load conditions, and implicated more dorsal prefrontal circuitry. In contrast, the AG group did not show this relationship, and employed more premotor, motor, posterior attentional, and subcortical circuitry related to performance. The two genotypes used different circuitry to achieve the same level of performance. In a second analysis involving the legacy PET data set of 28 schizophrenic patients for a single SNP such as DRD1-Ddel, the UCI team performed a GLM analysis of the effect of the genotype on the PET imaging phenotype (e.g., the mean measures in the left inferior frontal gyrus). The AA genotype showed consistently greater metabolism during an attentional task in the several areas compared to the AG or GG genotypes. The consistency between the results from PET and fMRI on the same subjects is being investigated.

Attentional Circuits in Schizophrenia as revealed by fMRI and PET (UCI) This project is using structural equation modeling to compare attentional circuitry within the legacy set of 28 schizophrenic subjects who performed similar attentional tasks in both a PET and fMRI scan. The data have been analyzed and segmented into a Talairach-based analysis. The mean glucose metabolism has been measured in the PET data on a region-by-region basis and the mean contrast values in the same regions have been measured in the fMRI data. A structural equation model is being defined for comparison between the two data sets. However, the segmentations are crude at best, and once the methods have been implemented on these regions, a second analysis using the improved segmentation methods will be implemented using the NA-MIC Toolkit derived segmentations.

Key Investigators

• **Harvard-BWH (PNL)** Martha Shenton, Marek Kubicki **(SPL)** Raul San Jose, Gordon Kindlmann, Wendy Plesniak, Sandy Wells, Carsten Richter, Haiying Liu, Cindy Wible, Ron Kikinis
• **Dartmouth** Andrew Saykin, Robert Roth, John West, Laura Flashman, Thomas McAllister, Nancy Koven, J.C. Pendergrass
• **GE** Jim Miller
• **GATech** Steven Haker, Allen Tannenbaum
• **Harvard-MGH** Dave Tuch, Josh Snyder
• **Isomics** Steve Pieper
• **Kitware** Karthik Krishnan
• **MIT** Polina Golland, Wanmei Ou
• **Toronto** James Kennedy
• **UCI** Steven Potkin, James Fallon, Jessica Turner, Lisa Kilpatrick, David Medina

Additional Information

For details of each of the projects in this theme, please see [[NA-MIC_Internal_Collaborative_Projects#fMRI Analysis|NA-MIC Projects on Functional MRI Analysis]].

Theme 4: THE NA-MIC KIT

Research Progress

The vision of the NA-MIC Kit is to provide an Open Source set of software tools and methodologies that will serve as the foundation for medical image computing projects for both academic and commercial use. Key elements of this vision are:

• ***Unrestrictive License*** Users of the Kit are free to distribute their derived works under any license suitable to their needs.
• ***Cross Platform*** This software set can be adapted to the best available price-performance computer systems for any particular use.
• ***Sophisticated User Interfaces*** Application domain scientists can interact efficiently with complex algorithms while leveraging their experience with common desktop computer software.
• ***Extensible Algorithmic Framework*** New techniques can be quickly integrated into a working system without tedious and error prone re-implementation of core functionality.
• ***Consistent and Manageable Engineering Methodology*** Developers and users can rely on accurate and well documented behavior from all the parts of the Kit.
• ***Creation of a Sustainable Community*** Users are actively involved in the design process of the Kit. Documentation, training materials, and hands-on sessions are available and well publicized to the community.

NA-MIC is assembling software that reflects these qualities and dedicating the Center's resources to transform satisfactory components to 'Best of Breed' solutions to meet the challenges of the medical image computing community. While focusing first on the needs of our DBP users, the integration of the NA-MIC Kit tools and the enhancements currently under way will have broader applicability to other image analysis domains within biomedical computing.

Research Progress

NA-MIC Software Process
The significant development effort of participating sites is reflected in the activities described in the NA-MIC Programming and Projects weeks, reported below under "Highlights." A major deliverable associated with this ongoing development is 3D Slicer version 3, also known as Slicer3. This tool assembles the NA-MIC Kit elements into a modern end-user application environment. It is important to note that the pieces of Slicer3 are designed for multi-use, and many of these pieces are expected to have significant use outside Slicer3.

CMake/CTest/CPack and Dart2 While the CMake and CTest portions of this software suite existed before NA-MIC and are currently being enhanced, CPack represents a new effort specifically developed to address the needs of the computing community using Slicer3 as a driving initial application. CPack provides a cross-platform mechanism for installing software applications using the native facilities of the target system (e.g., the InstallShield mechanisms on Windows or RPM packages for RedHat Linux). Dart2 is a second generation database-backed web server used to collate the results of software testing and provide sophisticated presentation models that permit developers to isolate software quality issues quickly across literally dozens of combinations of computer systems, compilers, and support libraries.

KWWidgets This free, cross platform user interface toolkit is undergoing significant enhancement as part of the NA-MIC effort. After extensive review of alternative UI tools, KWWidgets was adopted as the standard for the NA-MIC Kit. Efforts over the past year have been directed not only to delivering these enhancements, but also on educating the NA-MIC developer community in the most effective ways to use and extend KWWidgets.

Execution Model A major implication of the "Extensible Algorithmic Framework" design goal is the need to support a well defined and reusable pathway for implementation of new code. The Slicer3 Execution Model supports this goal by providing a methodology by which algorithms implemented as standard ITK classes can be used as either command line executables or as components of an interactive point-and-click environment without extensive rewriting by the algorithm developer. By adopting a standard XML syntax for expessing the options for an algorithm, the Framework can provide a set of tools to help the developer automatically make programs with

compatible syntax; the Framework also helps programs like Slicer3 interface to these command line executables in a consistent manner.

Software Infrastructure
The NA-MIC Kit builds on tools used widely in the community. Over the past year, our efforts have been focused principally on the integration and critical enhancement of these tools.

License Unification After extensive discussion and review, NA-MIC selected three categories of software licensing for the NA-MIC Kit:

- BSD-compatible software licenses are required for core pieces of the NA-MIC Kit.
- NA-MIC Kit software can rely on licensed libraries to allow static linking of executables, but is otherwise licensed under the LGPL.
- Support tools (compilers, debuggers, etc.) can be licensed under any Open Source license.

Software developers are encouraged to consider the implications of creating derived works from software in any of these three categories and to abide by the terms and conditions of each license.

This policy assures developers who create derived works based on the NA-MIC Kit that they will have the flexibility to select the appropriate software license for that work. For example, this policy would permit academic users to distribute binary-only versions of software in advance of publication or commercial users to incorporate parts of the NA-MIC Kit into their products.

Ownership of contributions to the NA-MIC Kit remains with the party that contributes them (that is, the authors or institutions that developed the contributions still hold the copyright). However, for these to be included in the NA-MIC Kit, the contribution must be made available under licensing terms compatible with the intended use, as described above.

ITK As a core set of image processing, segmentation, and registration C++ code, ITK has achieved remarkable world-wide acceptance and widespread use in advanced applications. Within the NA-MIK Kit, ITK is the standard method for Core 1 contributors to computationally express their algorithmic innovations. To address the needs of our DBPs, ITK has been enhanced by NA-MIC to include native support for image direction information, diffusion-weighted images (DWI), diffusion tensor images (DTI), and variable length vector valued images. In addition, new statistical code has been added to support the needs of fMRI analysis in ways that have not been available in any other numerical library meeting our licensing requirements. All the enhancements made by NA-MIC are contributed back to the ITK community to benefit other projects.

VTK VTK is the "de facto" standard for visualization in medical imaging as well as a wide range of application domains. As a mature system, VTK has not required extensive reworking to meet the needs of the NA-MIC Kit, but NA-MIC has benefited from the significant improvements made available by the VTK community. Recent examples include the addition of sophisticated interactive 3D Widgets, hardware accelerated volume rendering, and improved pipeline infrastructure. As a sophisticated user of this technology, NA-MIC provides feedback to the VTK developers on enhancements and usability; in particular, the release of version 5 of VTK exposed interoperability and backwards compatibility issues, which NA-MIC is helping to address, to the benefit of the entire development community.

3D Slicer

In the NA-MIC Kit end-user application software environment, improvements to VTK and ITK are made directly available to application scientists. Examples of these improvements from the past year include:

- ITK-based image I/O capability allowing read/write of a wide variety of raw and compressed image file types,
- ITK linear and non-linear image registration tools,
- Support for DWI and DTI images in the emerging standard NRRD file format,
- A host of engineering improvements including bug tracking, nightly builds, improved test scripts, and other general software engineering.

In the past year these and other 3D Slicer improvements have been disseminated through release of Slicer versions 2.5 and 2.6, respectively. These updates have been featured in several educational events conducted by the Training and Dissemination Cores.

Slicer 3 Base Development The NA-MIC development group, with representation from user communities, algorithm developers, and toolkit developers, has provided the ideal medium for a substantial re-work of the Slicer application. Dubbed Slicer3, this effort involves the migration of Slicer functionality into the newer generation of tools including CPack, KWWidgets, the Execution Model, and other NA-MIC and non-NA-MIC technologies. The Slicer3 Base comprises a layered collection of software consisting of:

- a Data Model supporting multiple undo/redo and a hierarchical linear and non-linear tranformation structure, together with XML serialization/deserialization capabilities;
- a set of Logic Classes that operate on the data model using VTK and ITK classes
- a set of GUI Classes consisting of composites of standard and custom KWWidgets and the code to apply user actions to the Logic and MRML structures.

The Slicer3 Base code uses a modern Command/Observer design pattern to ensure that there are no code dependencies between, for example, the data model and the logic classes that manipulate them. Slicer3 also takes advantage of the collective experience of the NA-MIC development group in the design and implementation of the coordinate system management code, which is an area that is often poorly or incompletely implemented in medical image computing codes.

Pipeline and Grid Interfaces

The strategy adopted by NA-MIC is to treat the Pipeline and Grid interfaces in as modular a fashion as possible but using the same Execution Model Framework described above as the basis for interactions between the Grid and Pipeline resources and the Slicer3 environment. This approach exposes the functionality to the end user as a seamless extension of the functionality running locally. Ongoing development will be required to make these diverse elements adhere to the standard environment.

Grid Computing Interface The NA-MIC community makes regular use of the Data Grid functionality provided through collaboration with the Biomedical Informatics Research Network (BIRN) collaboration. Data sets from the DBP groups are uploaded to the BIRN for sharing and analysis by NA-MIC Core 1 and Core 2 researchers using one of the several data access interfaces provided by BIRN (web interface, command line tools, and/or a Java-based programmatic interface). A new set of tools under development called 'gi' (for Grid Interface) provides a wrapper around the community-standard Condor grid tools for use by NA-MIC.

LONI Pipeline As envisioned in the original NA-MIC proposal, work has been ongoing to both access Slicer-based functionality from within the LONI Pipeline and to access LONI Pipeline functionality from Slicer. This level of interoperability is being achieved by adopting a common argument syntax for all command line execution modes for new Slicer modules and for the pipeline client, itself.

Upcoming NA-MIC Kit Milestones

We anticipate that much of the base functionality of Slicer3 and the aspects of the related projects needed by Slicer3 will be substantially completed during calendar year 2006. At the January 2007 NA-MIC All-Hands meeting, we plan to begin end-user training sessions, exposing DBP researchers and other users to the new code. By this point, significant portions of the ITK-based NA-MIC Core 1 algorithm development is expected to be usable directly within Slicer3. Over the course of 2006, there will be periodic release of alpha and beta development versions of Slicer3 to the development community as well as periodic developer meetings to work out specific design challenges. In particular, the summer NA-MIC Programmer/Project week in June of 2006 will include several projects aimed at completing substantial portions of Slicer3. The entire development process, including the source code repository, will remain publicly accessible so that end users and collaborators can monitor progress.

Training and Dissemination
NA-MIC is committed to developing a robust, sustainable community of developers and users for the NA-MIC Kit. Significant effort and resources have been dedicated to developing training material and conducting workshops and tutorials. A carefully selected set of target audiences and venues has been used to ensure that this material is available to the groups most likely to benefit from current NA-MIC Kit technology. In addition, all materials including software, data, training presentations, and even participant feedback are made publicly available on the NA-MIC wiki for the benefit of the community. These resources serve as a gateway through which potential new users are introduced to the richness of the NA-MIC Kit resources. The NA-MIC leadership and other participants are encouraged to provide pointers to these pages when presenting or interacting with potential users or collaborators. These resources are the critical part of our dissemination and training strategy.

Key Investigators
- **GE** Bill Lorensen, Jim Miller, Xiaodong Tao, Dan Blezek
- **Isomics** Steve Pieper, Alex Yarmarkovich
- **Kitware** Will Schroeder, Luis Ibanez, Karthik Krishnan, Andy Cedilnik, Sebastien Barre, Mathieu Malaterre
- **UCLA** Mike Pan, Jagadeeswaran Rajendiran
- **UCSD** Brendan Faherty, Jeff Grethe
- **Harvard-BWH (SPL)** Nicole Aucoin, Katie Hayes, Wendy Plesniak, Mike Halle, Gordon Kindlmann, Raul San Jose, Haiying Liu, Ron Kikinis
- **MIT** Lauren O'Donnell, Kilian Pohl

Link to Additional Information

For details of each of the projects in this theme, please see [[NA-MIC_Internal_Collaborative_Projects#NA-MIC Kit|NA-MIC Kit Projects]].

Highlights of Second Year Accomplishments
Although NA-MIC had a productive year as evidenced by its collaborative wiki (700 pages total, 200 users, 650K page views and 15K edits) and prolific publication, we have chosen to highlight three areas of achievement that exemplify the diversity of the NA-MIC collaborative. These selected accomplishments demonstrate the world-class software process used to create, implement, test and disseminate NA-MIC software (Cores 1,2,4,6); the on-going collaboration between the DBP scientists and algorithms scientists (Cores 1 and 3); and the on-going efforts to transition the new technology to researchers worldwide (Cores 4,5,6).

Before describing these highlights, one activity, in particular, epitomizes the culture of collaboration and technical excellence embodied in NA-MIC. In the first year of this National Center for Biomedical Computing (NCBC), NA-MIC established what was originally called "Programming Week," which brought together geographically and professionally diverse members from NA-MIC's multiple cores. The original con-

cept was to create teams from representatives of multiple cores, with experience levels ranging from expert to student. Each team identified technical challenges within NA-MIC's mandate and worked together for an intensive period ranging from an afternoon to an entire week. The ultimate goal of each project was to move from research problem to solution; with the solution implemented in our open source NA-MIC Kit software suite.

The results of this experiment have been strongly positive. Participants have been energized by the diversity of the teams and the rapid transition from research to implementation. In particular, the open source software process resulted in technology transition that was measurable in days or weeks versus the months or years that conventional processes require. The enthusiastic reception of Programming Week led NA-MIC to repeat this experiment several more times, with growing enthusiasm each time. We have also changed the name to "Project Week" to better reflect the extent of its activities and to emphasize NA-MIC's inter-Core focus on solving problems and transitioning results.

Highlight 1: The NA-MIC Software Process

According to the [http://www.nih.gov/about/director/060399.htm "The Biomedical Information Science and Technology Initiative (BISTI)"] report:

> ''One important element in the system is the creation of software-development groups: software and computer engineers who can take laboratory-based software and "harden" it; standardizing it for more general use, testing it under various conditions, documenting it, supporting it, and upgrading it as technology changes."
>
> '

'With this mandate in mind, NA-MIC has and continues to implement a world-class software process. At the core of this process is a minimally intrusive but effective set of procedures that have been developed over more than a decade, and which has been extended through the NA-MIC initiative into new areas. The process involves continuous testing software across multiple computing platforms (i.e., a computing platform is defined here as a combination of hardware, operating system, and compiler). The results of these tests are reported continuously on quality dashboards (see http://public.kitware.com/dashboard.php and choose the various software tools from the top tabs). Such feedback enables developers to make changes to the code base insuring that the quality of the software remains high. As evidenced by this [http://public.kitware.com/dashboard.php page], the various components making up the NA-MIC Kit, ITK, VTK, Slicer3.0, CMake, KWWidgets and other NA-MIC utilities--have all been placed under the auspices of the software process. The following paragraphs summarize the major accomplishments related to the software process in Year 2 of the NA-MIC effort.

- The next generation testing process, based on the DART server and CMake/CTest client, has been completed. DART now supports dynamic queries to a

formal database with configurable presentation of testing results and optimal storage strategies for managing the gigabytes of data arriving from testing clients around the world. CTest, which is an adjunct module to the CMake cross-platform build system, has been modified to integrate with the new DART server.

- CPack, a new software tool funded under the NA-MIC initiative, is another adjunct module to CMake. CPack is a cross-platform packaging and distribution utility that is an essential part of the NA-MIC software kit. CPack enables software to be easily packaged for distribution across computer platforms. Thus it is relatively easy to create binary and source code distributions for Windows, Linux, Unix and MacOSX systems. The ultimate effect is that the time to move from algorithm to software implementation to multi-platform distribution has been greatly reduced.

- [http://www.cmake.org CMake] release 2.4 has been completed. CMake enables software to be compiled, linked, and tested across multiple computer platforms. CMake is one of a few, and possibly only, build systems in the world today that can handle the complexity of configuring, building, and linking the NA-MIC software kit across multiple computing platforms. Thus CMake enables NA-MIC developers to rapidly combine advanced software toolkits such as VTK, ITK, and KWWidgets into complex software applications such as Slicer3.0.

As evidence of the effectiveness of the process, software communities around the world are now adopting the NA-MIC process for their own development efforts. For example, the [http://www.kde.org/ KDE Linux Desktop System], which is the world's largest open source software project in terms of lines of code, has adopted CMake as their official build tool. This choice was made by the KDE community after an intensive evaluation period which concluded that CMake is the only system in the world capable of managing KDE's complex build process. The KDE community is also enthusiastically embracing the testing quality dashboards.

Highlight 2: Clinical Application of Diffusion Tensor Imaging

MIT computer scientists, in collaboration with Harvard neuroscientists, have produced a robust method for identifying anatomically distinct fiber tracts in the human brain using clustering techniques applied to magnetic resonance diffusion tensor imaging (DTI). DTI is a relatively new technique that makes it possible to visualize and quantify the organization and integrity of white matter fiber tracts in the brain, in vivo. As part of the NA-MIC collaboration, the focus is on identifying fiber tracts that may be abnormal in schizophrenia, although such work can be applied to study both global and specific diffusion changes in white matter in various neurologic and psychiatric disorders including Alzheimer's disease and multiple sclerosis. Of note here, MIT computer scientists have worked closely with schizophrenia researchers to develop and apply sophisticated computer vision algorithms to extract fiber bundles likely to be important in the pathophysiology of schizophrenia, including the fornix,

uncinate fasciculus (the largest fiber tract connecting the frontal and temporal lobe), and the corpus callosum (largest white matter fiber tract in the brain and likely important in communication between the two hemispheres). The method developed can also be applied to surgical planning, to clinical psychiatry, as well as to neurologic disorders and for identifying fiber bundles in the brain.

The paper, "A Method for Clustering White Matter Fiber Tracts," will appear in the May issue of the American Journal of Neuroradiology. This work was funded by NA-MIC. Illustrating the cross-disciplinary nature of NA-MIC, an MIT computer scientist is the first author on this paper with collaborators from Harvard and the Veterans Administration. Thus NA-MIC has successfully teamed computer scientists and software engineers to create industry quality software tools to solve DBPs.

Highlight 3: Outreach

Outreach in NA-MIC consists of a joint effort between the Training, Dissemination, and Service Cores. The primary outreach goal of the center in its second year was to focus on the broader research community. This was accomplished using several mechanisms. Eleven training workshops were held that provided hands-on training to over 300 participants in the use of the NA-MIC kit, an open source workshop was organized in conjunction with a major medical image computing conference, MICCAI, and two birds-of-a-feather meetings were held. Three invited talks were presented about NA-MIC and the wiki-based collaborative web presence was also approximately doubled in this time. The rest of this section provides details of these outreach activities.

Training Materials and Workshop This year we delivered over 300 slides as part of 8 self-guided tutorials that include pre-processed, anonymous data sets on our Slicer 101 web page that had over 2000 hits in 200 days. More than 300 people attended the 11 workshops we offered this year at local NA-MIC sites, national conferences, and international meetings.

First International Training Workshops A workshop was organized in response to a request by researchers at EPFL, Lausanne, Switzerland who were interested in advanced development using our software tools. Thirty-seven participants from 9 countries attended this 2.5-day hands-on event at EPFL. Details of this workshop are available at : http://www.na-mic.org/Wiki/index.php/Dissemination:EPFL_Workshop_2005

Open Source Workshop in conjunction with MICCAI 2005 A workshop on open source software, a driving theme in the NA-MIC kit, was held in conjunction with MICCAI 2005 in Palm Springs, CA. There were 80 registered attendees for this workshop, 37 submissions, 90 open reviews, and 21 submissions were selected for presentation. This workshop was organized jointly with the Insight Software Consortium and details are available here: http://www.na-

mic.org/Wiki/index.php/Dissemination:MICCAI_Workshop_2005

Validation Workshop A workshop on the topic of validation was held in conjunction with the NA-MIC all-hands meeting in Salt Lake City, Utah in January, 2006. There were over 50 participants in this workshop, primarily from within NA-MIC and some outside collaborators. Details of this workshop are available here: http://www.na-mic.org/Wiki/index.php/AHM2006_ValidationWorkshop

Invited Talks Three invited talks were also given about NA-MIC at CSB, Stanford (Kikinis, Aug 2005), Schizophrenia and Big Science (ISBI, March 2006), NA-MIC Kit (Pieper, 2006).

Birds-of-a-Feather Meetings The "Programming Week" event that was started in the first year of NA-MIC to gauge the interest of participants in spending a week together working on NA-MIC projects was expanded in both scope and duration in the second year. The forum was expanded to include algorithm brainstorming and clinical application work, and the event was re-named "Project Week" to reflect this change. The duration has been extended to 1.5 weeks per year – the last week of June at MIT, as well as half a week in conjunction with the all-hands meeting in January. The extension in duration has largely been to accommodate the desire of the participants to stay in touch with the community.

Web Presence The collaborative wiki (http://wiki.na-mic.org) has expanded to 700 pages and about 200 users. (In the first year, we had 350 pages and 150 users.) Since the inception of this wiki, there have been a total of 650K page views and 15K page edits, which translates to 4 edits per page and 41 views per edit. In addition to the NA-MIC investigators, the usage of this web page by external collaborators continues to expand (NAC, NCIGT, and CIMIT were added this year, while NIH and BIRN continue to use it from last year).

Performance Evaluation and Software and Data Integration Working Groups

During the past year, the leadership core has been actively participating in the performance evaluation and software and data integration discussion of the seven NCBCs. The Software and Data Integration Working Group (SDIWG) is coordinated by Peter Lyster of NIGMS. In concert with the project teams and Centers' staff, the goals of the SDIWG are to: advance the domain sciences, promote software interoperability and data exchange, and to capture the collective knowledge of software engineering and practices among the NCBCs and publish this knowledge widely. In addition, the NCBC Evaluation Group, spearheaded by Chuck Friedman of the National Library of Medicine (NLM), evaluates the performance of the NCBCs across all seven Centers, as well as individual Center performance. Stephen Wong, PI of the NA-MIC Management Core, has continued to participate as the liai-

son to the NCBC Evaluation Committee for the past year. He attended the regular evaluation TCONs and was involved in drafting the big 'P' evaluation document, selecting external consultants, and planning the NCBC evaluation workshops.

Interaction with other Centers for Biomedical Computing

Bill Lorensen, PI of NA-MIC Engineering Core, is the NA-MIC representative to the Software and Data Integration Working Group. This group meets monthly to discuss interoperability and data exchange between the Centers. Lorenson has participated in these regular monthly teleconferences (TCONs) to discuss the strategy and sharing of various tools and pipelines developed with the Centers.

The highlights of these TCONs can be found in http://www.na-mic.org/Wiki/index.php/SDIWG:Software_Engineering_Body_of_Knowledge_Across_NCBC_Biocomputing_Centers.

Lorensen has also been active in the formulation of a vision and requirements for a cross-Center Yellow Pages. This mechanism will be a framework for organizing and distributing information about software generated by the Centers.

Additionally, Lorensen participated in a Workshop on the "Ontology of Images" sponsored by the Stanford Center for Biological Ontologies. Lorensen also gave a talk, "Beyond Pixels," that described a methodology for connected segmented medical images to the University of Washington Foundational Model of Anatomy ontology. He also participated on a panel discussion "Ontologies versus Yellow Pages."

Impact and Value to Biocomputing

NA-MIC's impact on biomedical computing accelerated in this second year of its existence. The NCBC RFA stated: "The NIH NCBC will be devoted to all facets of biomedical computing, from basic research in computational science to providing the tools and resources that biomedical and behavioral researchers need to do their work." and "...the NIH NCBC will play a major role in educating and training researchers to engage in biomedical computing."

The Center's tools, resources, and processes are having an impact within the Center, within NIH, and at the national and international level. NA-MIC is becoming a resource for biomedical open source software and open source software processes.

Impact within the Center Within the Center, Core 2 has introduced the NA-MIC software process to basic researchers in Core 1. Skills such as revision control, software testing, and object-oriented design are not usually part of a basic research curriculum. Good software engineering skills are critical for translating algorithms into usable, robust software for end-users. As stated in the original NA-MIC proposal, "Core 2 is the link between the innovative techniques of Core 1 and the biological

questions of the Core 3 end-user practitioners. To build this link, Core 2 will establish software architectures and software processes that will empower the Core 1 algorithm developers to create robust, well-designed software and interfaces."

The Center has established a nightly build and test process for Slicer2 that has extended the number of platforms supported by Slicer from two (Solaris and Windows) to six.

Although 3D Slicer is the delivery platform for the Center, there are many supporting toolkits and support tools. These have been packaged as the NA-MIC Kit. Components of the NA-MIC kit follow the NA-MIC development process or an equivalent process. Key to this effort is the adoption of software licenses that adhere to open source rules and do not restrict usage of the software. The newly created Slicer License balances open source access and clinical restrictions and serves as a model for future clinically oriented open source projects.

Impact within NIH Funded Research NIH projects are starting to adopt NA-MIC pioneered processes and tools. NA-MIC hosts wikis for the Morphology Birn (mBirn) and the Function Birn (fBirn). Both of these NIH-funded programs are using the wikis to organize and disseminate the agendas of their All-Hands Meetings. The word of NA-MIC's successful Programmer/Project week has reached beyond the Center. The fBirn, at its recent all-hands meeting in Irvine, decided to hold a similar event in June 2006 to have the Birn Coordinating Center (Birn CC) work with fBirn developers on fBirn specific adaptation of Birn CC tools. The University of Iowa has adopted CMake, CTest, and Dart 2 to coordinate nightly builds and tests for the Neuroimaging Informatics Technology Initiative (NIFTI). Through outreach activities, NA-MIC PI's have promoted the open, collaborative and distributed software process pioneered by NA-MIC. The outreach activities within NIH included the NIH P41 Principal Investigator's Meeting, the Wadsworth Center's P41 "Resource for the Visualization of Biological Complexity" and UConn's P41 "National Resource for Cell Analysis and Modeling". NA-MIC is becoming a resource for NIH groups interested in open sourcing biomedical software.

Local, Regional, National and International Impact The NA-MIC software includes existing toolkits that are supported by open source software communities. ITK, the Insight Toolkit, was originally funded by the NLM. NLM funding is now limited to maintenance. NA-MIC has provided new ITK functionality to support the Center's requirements for Diffusion Tensor Imaging and Functional MRI. This new software fills the needs of NA-MIC but also provides ITK's international community with valuable new technology.

NA-MIC's software process also has national impact. Dart/Ctest has been adopted by many national and international open software development groups. For example, CMake has been adopted by the K Desktop Environment (KDE). This graphical desktop environment for Linux and Unix workstations is one of the largest open source projects in the world.

The NA-MIC All-Hands Meeting welcomed attendees from outside the Center including Northwestern, UIowa and the MIND Institute. The Programmer/Project Weeks had participants from UIowa, SRI, and the SCI Institute.

NA-MIC co-sponsored an Open Source Workshop at the 2005 MICCAI conference attended by 80 participants, far exceeding expected numbers. The proceedings of the workshop were published in the electronic Insight Journal, another NIH-funded activity. A workshop on Advanced ITK and Slicer was held at the Swiss Federal Institute of Technology (EPFL), Lausanne, Switzerland.

NA-MIC Timeline

This section provides a table of NAMIC timelines from the original proposal that graphically depicts completed tasks/goals in years 1 and 2 and tasks/goals to be completed in years 3-5. Changes to the original timelines have also been described. These tables demonstrate that the project is, on the whole, proceeding according to the originally planned schedule."'

CORE 1: Algorithms

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
MIT	1	SHAPED-BASED SEGMENTATION		
	1.1	Methods to learn shape representations	Year 2	Completed
	1.2	Shape in atlas-driven segmentation Year 4	Year 4	Partially completed, preliminary results
	1.3	Validate and refine approach	Year 5	Partially completed, preliminary results
MIT	2	SHAPE ANALYSIS		
	2.1	Methods to compute statistics of shapes	Year 4	Partially completed, software framework
MIT	3	ANALYSIS OF DTI DATA		
	3.2	Fiber statistics	Year 4	Partially completed, tract clustering
Utah	1	Processing of DTI data		
	1.1	Filtering of DTI	Year 2	Completed
	1.2	Quantitative analysis of DTI	Year 3	Completed partially, ongoing
	1.3	Segmentation of cortex/WM	Year 3	Completed partially, ongoing
Utah	2	CORTICAL SURFACE MATTER		
	2.1	Filtering and feature detection	Year 1	Incomplete, ongoing
Utah	3	FAST IMPLEMENTATION PDES	Year 4	Incomplete, ongoing
UNC	1	STATISTICAL SHAPE ANALYSIS		
	1.1	Comparative analysis of shape analysis schemes	Year 2	Completed

CORE 1: Algorithms (continued)

	1.3	Statistical shape analysis including patient variable	Year 5	Completed
UNC	2	STRUCTURAL ANALYSIS OF DW-MRI		
	2.1	DTI tractography tools	Year 4	Completed
	2.2	Geometric characterization of fiber tracts	Year 5	Completed
	2.3	Quantitative analysis of diffusion along fiber tracts	Year 5	Completed
GATech		ITK implementation of PDEs	Year 2	Completed
		Applications to Core 3 data	Year 4	Results and ongoing
		New statistic models	Year 4	Completed, preliminary results

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
MGH	1	REGISTRATION		
	1.1	Collect DTI/QBALL data	Year 2	Completed
	1.2	Develop registration method	Year 2	Completed
	1.3	Test/optimize registration method	Year 3	In progress
	1.4	Apply registration on core 3 data	Year 5	In Queue
MIT	2	GROUP DTI STATISTICS		
	2.1	Develop group statistic method	Year 2	Completed
	2.2	Apply on core 3 data	Year 5	In Queue
MGH	3	DIFFUSION SEGMENTATION		
	3.1	Collect DTI/QBALL data	Year 2	Completed
	3.2	Develop/optimize segmentation Algorithm	Year 3	Partially completed
	3.3	Integrate w/ tractography	Year 4	Partially Completed
	3.4	Apply on core 3 data	Year 5	In Progress

TIMELINE MODIFICATIONS CORE 1

GROUP	AIM	MILESTONE	MODIFICATION
MIT	2.4	Plan to develop software infrastructure to integrate shape analysis tools into the pipeline for population studies.	New
MIT	4	PLANS TO FOR FMRI DEVELOPMENT INCLUDING LOCAL AND ATLAS-BASED PRIORS FOR QUANTIFYING ACTIVATION.	New

(TIMELINE MODIFICATIONS CORE 1 CONT.)

Utah	2.2	Feature-based brain image registration.	Shift emphasis to shape-based analysis/registration
UNC	1.2	Develop medially-based shape representation	Remove
UNC	2.4	DTI Atlas Building (Years 2--4)	New
GaTech		Shape analysis	New

CORE 2: Engineering

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
GE	1	DEFINE SOFTWARE ARCHITECTURE		
	1.1	Object design	Year 1	Completed
	1.2	Identify patterns	Year 3	On schedule, ongoing
	1.3	Create frameworks	Year 3	On schedule, ongoing
GE	2	SOFTWARE ENGINEERING PROCESS		
	2.1	Extreme programming	Year 1-5	On schedule, ongoing
	2.2	Process automatiion	Year 3	On schedule, ongoing
	2.3	Refactoring	Year 3	On schedule, ongoing
GE	3	AUTOMATED QUALITY SYSTEM		
	3.1	DART deployment	Year 2	Complete
	3.2	Persistent testing system	Year 5	Incomplete
	3.3	Automatic defect detection	Year 5	Incomplete
Kitware	1	CROSS-PLATFORM DEVELOPMENT		
	1.1	Deploy environment (CMake, CTest)	Year 1	Complete
	1.2	DART Integration and testing	Year 1	Complete
	1.3	Documentation tools	Year 2	Complete
Kitware	2	INTEGRATION TOOLS		
	2.1	File Formats/IO facilities	Year 2	Complete (ongoing)
	2.2	CableSWIG deployment	Year 3	Complete (integration ongoing)
	2.3	Establish XML schema	Year 4	Incomplete
Kitware	3	TECHNOLOGY DELIVERY		
	3.1	Deploy applications	Year 1	Complete (ongoing)
	3.2	Establish plug-in repository	Year 2	Incomplete
	3.3	Cpack	Year 4-5	Incomplete
Isomics	1	NA-MIC BUILDS OF SLICER	Years 2-5	Complete
	1.1	Schizophrenia and DBP intefaces	Year 3-5	Partially completed, ongoing
	2	ITK INTEGRATION TOOLS	Year 1-3	Completed
	2.1	SLIPIE integration	Year 2-4	Completed

CORE 1: Algorithms (continued)

	2.2	fMRI/DTI algorithm support	Year 2-5	Completed DTI, fMRI Ongoing
	2.3	New DBP algorithm support	Year 2---5	Ongoing
Isomics	3	COMPATIBLE BUILD PROCESS	Year 1-3	Completed
	3.1	Dart Integration	Year 1-2	Completed, upgrades
	3.2	Test scripts for new code	Year 2-5	Ongoing
UCSD	1	GRID COMPUTING-BASE	Year 1	Completed
	1.1	Grid enabled algorithms	Year 3	Ongoing
	1.2	Testing infrastructure	Year 4	Initiated
	2	DATA GRID - COMPATIBILITY	Year 2	Completed
	2.1	Data grid -slicer access	Year 2	In progress
	3	DATA MEDIATION - DEPLOY	Year 1	Incomplete (modfication below)
UCLA	1	DEBABELER FUNCTIONALITY	Year 1	Continued Progress
	2	SLIPIE INTERPRETATION (LAYER 1)	Year 1 - 2	In Progress
	3	SLIPIE INTERPRETATION (LAYER 2)	Year 1-2	On Schedule
	3.1	Developing ITK Modules	Year 2	In Progress
	4	INTEGRATING SRB (GSI-ENABLED)	Year 2	Completed
	5	INTEGRATING IDA	Year 2	Completed
	5.1	Integrating External Visualization Applications	Year2	Completed

TIMELINE MODIFICATIONS CORE 2

GROUP	AIM	MILESTONE	MODIFICATION
Isomics	3	DATA MEDIATION	Delayed pending integration of databases into NAMIC infrastructure

CORE 3: Driving Biological Projects

THE CORE 3 PROJECTS SUBMITTED R01 STYLE PROPOSALS, AS SPECIFIED IN THE RFA, AND DID NOT SUBMIT TIMELINES

CORE 4: SERVICE

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
Kitware	1	IMPLEMENT DEVELOPMENT FARMS		
	1.1	Deploy platforms	Year 1	Complete
	1.2	Communications	Year 1	Complete, ongoing

CORE 4: Service (continued)

2	ESTABLISH SOFTWARE PROCESS		
2.1	Secure developer database	Year 1	Complete, ongoing
2.2	Collect guidelines	Year 1	Complete
2.3	Manage software submission process	Year 1	Complete
2.4	Configure process tools	Year 1	Complete
2.5	Survey community	Year 1	Complete
3	DEPLOY NAMIC TOOLS		
3.1	Toolkits	Year 1	Complete
3.2	Integration tools	Year 1	Complete
3.3	Applications	Year 1	Complete
3.4	Integrate new computing resources	Year 1	Complete
4	PROVIDE SUPPORT		
4.1	Esablish support infrastructure	Years 1-5	On schedule, ongoing
4.2	NAMIC support	Year 1	Complete
5	MANAGE NAMIC SOFTWARE RELEASES	Years 1--5	On schedule, ongoing

TIMELINE MODIFICATIONS CORE 4

GROUP	AIM	MILESTONE	MODIFICATION
Kitware	2-5	Various	Refined/modified sub aims

CORE 5: TRAINING

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
Harvard	1	FORMAL TRAINING GUIDLLINES		
	1.1	Functional neuroanatomy	Year 1	Complete
	1.2	Clinical correlations	Year 1	Complete
	2	MENTORING		
	2.1	Programming workshops	Years 1-5	On schedule, ongoing
	2.2	One-on-one mentoring, Cores 1, 2, 3	Years 1-5	On schedule, ongoing
	3	COLLABORATIVE WORK ENVIRONMENT		
	3.1	Wiki	Years 1	Complete

TIMELINE MODIFICATIONS CORE 5:

GROUP	AIM	MILESTONE	MODIFICATION	
Harvard	3.2	Mailing lists	Year 1	Complete
	3.3	Regular telephone conferences	Years 1-5	On schedule, ongoing
	4	EDUCATIONAL COMPONENT FOR TOOLS		
	4.1	Slicer training modules	Year 3	Complete
	5	DEMONSTRATIONS AND HANDS-ON TRAINING		
	5.1	Various workshops and conference	Years 1-5	On schedule, ongoing (see also link)

CORE 6: DISSEMINATION

GROUP	AIM	MILESTONE	PROJECTED COMPLETION	STATUS
Isomics	1	CREATE A COLLABORATION METHODOLOGY FOR NA-MIC		
	1.1	Develop a selection process	Year 1	Complete
	1.2	Guidelines to govern the collaborations	Years 1-2	Complete
	1.3	Provide on-site training	Years 1-5	On Schedule
	1.4	Develop a web site infrastructure	Year 1	Complete
	2	FACILITATE COMMUNICATION BETWEEN NA-MIC DEVELOPERS AND WIDER RESEARCH COMMUNITY		
	2.1	Develop materials describing NAMIC technology	Years 1-5	On Schedule
	2.2	Participate in scientific meetings	Years 2-5	On Schedule
	2.3	Document interactions with external researchers	Years 2-5	On Schedule
	2.4	Coordinate publication strategies	Years 3-5	On track
	3	DEVELOP A PUBLICLY ACCESSIBLE INTERNET RESOURCE OF DATA, SOFTWARE, DOCUMENTATION, AND PUBLICATION OF NEW DISCOVERIES		
	3.1	On-line repository of NAMIC related publications and presentations	Years 1-2-3	On Schedule
	3.2	On-line repository of NAMIC tutorial and training material	Years 1-5	
	3.3	Index and a searchable database	Years 1-2	Complete
	3.4	Automated feedback systems that track software downloads	Year 3	On track

APPENDIX A: PUBLICATIONS

Peer Reviewed Journal Papers

1. Nakamura M, McCarley RW, Kubicki M, Dickey CC, Niznikiewicz MA, Voglmaier MM, Seidman LJ, Maier SE, Westin CF, Kikinis R, Shenton ME. Fronto-temporal disconnectivity in schizotypal personality disorder: a diffusion tensor imaging study. Biol Psychiatry. 2005 Sep 15;58(6):468-78.
2. Tuch DS, Salat DH, Wisco JJ, Zaleta AK, Hevelone ND, Rosas HD. Choice reaction time performance correlates with diffusion anisotropy in white matter pathways supporting visuospatial attention. Proc Natl Acad Sci U S A. 2005 Aug 23;102(34):12212-7.
3. Tuch DS, Wisco JJ, Khachaturian MH, Ekstrom LB, Kotter R, Vanduffel W. Q-ball imaging of macaque white matter architecture. Philos Trans R Soc Lond B Biol Sci. 2005 May 29;360(1457):869-79.
4. Niethammer M, Vela P, Tannenbaum A. On the evolution of closed curves by means of vector distance functions. Int. Journal Computer Vision, 2006.
5. Niethammer M, Tannenbaum A, Angenent S. Dynamic active contours. IEEE Trans. Automatic Control. 2006; 51:562-579.
6. Turner JA, Smyth P, Macciardi F, Fallon JH, Kennedy JL, Potkin SG. Imaging phenotypes and genotypes in schizophrenia. Neuroinformatics. 2006;4(1):21-49.

In Press

1. Liu T, Young G, Huang L, Chen N-K, Wong S. "76-space Analysis of Grey Matter Diffusivity: Methods and Applications," in press, NeuroImage.
2. O'Donnell L, Kubicki M, Shenton ME, Dreusicke MH, Grimson WEL, Westin CF. A method for clustering white matter fiber tracts. AJNR (In Press).
3. Koo MS, Levitt JJ, McCarley RW, Seidman LJ, Dickey CC, Niznikiewicz MA, Voglmaier MM, Zamani P, Long KL, Kim SS, Shenton ME. Reduction of caudate volume in neuroleptic-naive female subjects with schizotypal personality disorder. Biol Psychiatry (In Press).
4. Kuroki N, Kubicki M, Nestor PG, Salisbury DF, Park HJ, Levitt JJ, Woolston S, Frumin M, Niznikiewicz M, Westin CF, Maier SE, McCarley RW, Shenton ME. Fornix integrity and hippocampal volume in male schizophrenic patients. Biol Psychiatry (In Press).
5. Onitsuka T, Niznikiewicz MA, Spencer KM, Frumin M, Kuroki N, Lucia LC, Shenton ME, McCarley RW. Schizophrenia is associated with functional and structural deficits in brain regions subserving face processing. Am J Psychiatry (In Press).
6. Niethammer M, Tannenbaum A, Kalies W, Mischaikow K. Detecting simple points in higher dimensions. IEEE Image Processing, 2006. (In Press).
7. Rathi Y, Dambreville S, Tannenbaum A. Comparative analysis of kernel methods for statistical shape learning. CVAMIA'06, 2006. (In Press).
8. Roth RM, Koven, NS, Randolph JJ, Flashman LA, Pixley HS, Ricketts SM, Wishart HA, Saykin AJ. Event-Related fMRI study of Functional magnetic resonance imaging of executive control in bipolar disorder. NeuroReport, 2006 (In Press).

Peer Reviewed Conference Proceedings
Conferences included here represent the major high quality conferences in medical image analysis (MICCAI, IPMI, MMBIA, ISBI). These conferences only accept submission of full papers and guarantee a peer review process by at least three reviewers and an area chair. Acceptance rates are below 40% for MICCAI, IPMI and MMBIA and around 50% for ISBI.

1. Xu S, Styner M, Davis B, Joshi S, Gerig G. Group Mean Differences of Voxel and Surface Objects via Nonlinear Averaging, IEEE Symposium on Biomedical Imaging. IEEE Symposium on Biomedical Imaging ISBI. 2006; 758-761.
2. Styner M, Jomier M, Gerig G: Closed and Open Source Neuroimage Analysis Tools and Libraries at UNC. IEEE Symposium on Biomedical Imaging ISBI. 2006; 702-705.
3. Gerig G, Joshi S, Fletcher T, Gorczowski K, Xu S, Pizer SM, Styner M. Statistics of populations of images and its embedded objects: Driving applications in neuroimaging. IEEE Symposium on Biomedical Imaging ISBI. 2006; 1120-1123.
4. Pieper S, Lorensen W, Schroeder W, Kikinis R. The NA-MIC Kit: ITK, VTK, Pipelines, Grids and 3D Slicer as An Open Platform for the Medical Image Computing Community. IEEE Symposium on Biomedical Imaging ISBI. 2006; 698-701.
5. Pichon E, Westin CF, and Tannenbaum A. A Hamilton-Jacobi-Bellman approach to high angular diffusion tractography. Proceedings of MICCAI, 2005.
6. Nain D, Haker S, Bobbick, A, Tannenbaum A. Multicale shape analysis using spherical wavelets. Proceedings of MICCAI, 2005.
7. Yang Y, Zhu L, Haker S, Tannenbaum A. On the harmonic skeleton and vessel data. Proceeedings of MICCAI, 2005.
8. Styner M, Gimpel Smith R, Cascio C, Oguz I, Jomier M. Corpus Callosum Subdivision based on a Probabilistic Model of Inter-hemispheric Connectivity. Medical Image Computing and Computer Assisted Interventions MICCAI. 2005 LNCS 3750;765-772.
9. Liu T, Young G, Huang L, Chen N-K, Wong S. "76-space Analysis of Grey Matter Diffusivity: Methods and Applications," MICCAI 2005.
10. Pichon E, Westin C-F, Tannenbaum A. A Hamilton-Jacobi-Bellman approach to high angular resolution diffusion tractography. Proc MICCAI, Oct 26-29 2005
11. Pichon E, Tannenbaum A. Curve segmentation using directional information, relation to pattern detection. Proc IEEE International Conference on Image Processing (ICIP), 2005
12. Nain D, Haker S, Bobick A, Tannenbaum A. Multiscale 3D Shape Analysis using Spherical Wavelets. Proc MICCAI, Oct 26-29 2005; p 459-467.
13. Corouge I, Fletcher PT, Joshi S, Gilmore JH, Gerig G. Fiber Tract-Oriented Statistics for Quantitative Diffusion Tensor MRI Analysis. Proc. MICCAI, Oct 26-29 2005; LNCS 3749, pp. 131-139
14. Ou W, Golland P. From Spatial Regularization to Anatomical Priors in fMRI Analysis. Proc IPMI, Jul 10-15 2005; LNCS 3565: p 88-100.

15. Pohl KM, Fisher J, Levitt JJ, Shenton ME, Kikinis R, Grimson WEL, Wells WE. " A Unifying Approach to Registration, Segmentation, and Intensity Correction," In Proc. MICCAI 2005: Eigth International Conference on Medical Image Computing and Computer Assisted Intervention, Palm Springs, CA, USA, Springer-Verlag, Part I, vol. 3749 of Lecture Notes in Computer Science, pp. 310-318, 2005
16. Pohl KM, Bouix S, Shenton ME, Grimson WEL, Kikinis R. " Automatic Segmentation Using Non-Rigid Registration," In short communications of MICCAI 2005: Eighth International Conference on Medical Image Computing and Computer Assisted Intervention, Palm Springs, CA, USA, 2005
17. Martin-Fernandez M, Bouix S, Ungar L, McCarley RW, Shenton ME. Two Methods for Validating Brain Tissue Classifiers. MICCAI 2005, Palm Springs, CA, USA: Duncan J and Gerig G (Eds.): Lecture Notes in Computer Science, volume 3749, pp 515-522, 2005. Springer-Verlag Berlin Heidelberg, 2005.
18. Kim S, Smyth P, Stern H, Turner J. Parametric response surface models for analysis of multi-site fMRI data. In Proc. MICCAI 2005: Eighth International Conference on Medical Image Computing and Computer Assisted Intervention, Palm Springs, CA, USA, Springer-Verlag, Part I, vol. 3749 of Lecture Notes in Computer Science, pp. 352-359, 2005.
19. O'Donnell L, Westin C-F. White Matter Tract Clustering and Correspondence in Populations. MICCAI 2005, Palm Springs, CA, USA: Duncan J, Gerig G (Eds.): Lecture Notes in Computer Science, volume 3749, pp 140-147, 2005. Springer-Verlag Berlin Heidelberg, 2005.

Book Chapters

1. Nain D, Tannenbaum A, Unal G, Yezzi A, Zeitouni O. On a stochastic model of geometric snakes. Mathematical Methods in Computer Vision: A Handbook, edited by Faugeras O, Paragios N, Springer-Verlag, 2005.
2. Angenent S, Tannenbaum A, Yezzi A, Zeitouni O. Curve shortening and interacting particle systems. Book chapter in a volume edited by Hamid Krim, 2005.

Insight Journal

1. Goodlett C, Corouge I, Jomier M, Gerig G. A Quantitative DTI Fiber Tract Analysis Suite. Insight Journal, 2005.
2. Miller JV. Probability distributions for the Insight Toolkit. Insight Journal, 2006.
3. Melonakos J, Krishnan K, Tannenbaum A. An ITK filter for Bayesian segmentation: itkBayesianClassifierImageFilter. Insight Journal, Jan 2006
4. Melonakos J, Al-Hakim R, Fallon J, Tannenbaum A. Knowledge-based segmentation of brain MRI scans using the Insight Toolkit. Insight Journal, Oct 2005.

Conferences and Workshops

1. Al-Hakim R, Fallon J, Nain D, Melonakos J, Tannenbaum A. A dorsolateral prefrontal cortex semi-automatic segmenter. SPIE Medical Imaging, 2006.
2. Eric Pichon, Delphine Nain, and Marc Niethammer. A Laplace Equation Approach for Shape Comparison. Proc SPIE Medical Imaging, 2006.
3. Al-Hakim R, Fallon J, Nain D, Melonakos J, Tannenbaum A. "A Dorsolateral

Prefrontal Cortex Semi-Automatic Segmenter." Proc SPIE Medical Imaging, 2006.
4. Pohl KM, Fisher J, Kikinis R, Grimson WEL, Wells WM. "Shape Based Segmentation of Anatomical Structures in Magnetic Resonance Images, " In Proc. ICCV 2005: Computer Vision for Biomedical Image Applications: Current Techniques and Future Trend, An International Conference on Computer Vision Workshop, Beijing, China, Springer-Verlag, vol. 3765 of Lecture Notes in Computer Science, 2005
5. Zöllei L, Learned-Miller E, Grimson WEL, Wells WM III. Efficient Population Registration of 3D Data. Proc ICCV 2005, Computer Vision for Biomedical Image Applications; Beijing, China
6. Angenent S, Pichon E, Tannenbaum A. Mathematical methods in medical imaging. Bulletin of American Mathematical Association, 2006.
7. O'Donnell L, Westin C-F. A High-Dimensional Fiber Tract Atlas. accepted to ISMRM 2006.

Submitted and in Preparation

1. Flashman LA, Roth RM, Pixley HS, Cleavinger HB, Saykin AJ, McAllister TW, Vidaver RM. (submitted). Cavum septum pellucidum in schizophrenia: Clinical and neuropsychological correlates.
2. Szymczak A, Tannenbaum A, Stillman A, Mischaikow K. Vessel cores from 3D imagery: a topological approach. submitted to IEEE Trans. Medical Imaging, 2006.
3. Michailovich O, Tanenbaum A. Fast approximation of smooth functions from samples of partial derivatives. Submitted for publication to IEEE Signal Processing, 2006.
4. Zhu L, Yang Y, Haker S, and Tannenbaum A. An image morphing technique based on optimal mass preserving mapping. Submitted to IEEE Trans. Image Processing, 2006.
5. Rathi Y, Vaswani N, Tannenbaum A, Yezzi Y. Particle filtering for continuous closed curves. Submitted to IEEE PAMI, 2005.
6. Rathi Y, Tannenbaum A. Kernel PCA for shape based segmentation of medical images. submitted to MICCAI, 2006.
7. Nain D, Haker S, Bobick A, Tannenbaum A. Shape-driven surface segmentation using spherical wavelets. Submitted to MICCAI, 2006.
8. Gorczowski K, Gerig G, Fletcher T, Pizer SM, Styner M. Statistics of Pose and Shape in Multi-Object Complexes using Principal Geodesic Analysis. submitted to MICCAI, 2006.
9. Goodlett C, Davis B, Jean R, Gilmore J, Gerig G. Improved Correspondence for DTI Population Studies via Unbiased Atlas Building. submitted to MICCAI, 2006.
10. Corouge I, Fletcher PT, Sarang J, Gouttard S, Gerig G. Fiber Tract-Oriented Statistics for Quantitative Diffusion Tensor MRI Analysis. submitted MedIA Journal, Jan. 2006
11. Gribbin M, Clement M, Muller K, Poe M, Cascio C, Jomier M, Piven J, Gerig G. Statistical analysis of diffusion tensor image data based on first principles, submitted
12. Flashman LA, Roth RM, Koven NS, McAllister TW, Vidaver RM, Pendergrass JC. Neural Correlates of Self-Evaluation in Individuals with Schizophrenia. in preparation.

APPENDIX B All of the investigators listed in this appendix made significant contributions to NA-MIC; however, not all of them were funded through NA-MIC. For funding details, please refer to the budget section of this Annual Report.

CORE 1: ALGORITHMS ROSS WHITAKER, CORE PI	CORE 2: ENGINEERING BILL LORENSON, CORE PI
University of Utah (Utah) **Ross Whitaker, Site PI** Sigash Awate Saurav Basu Joshua Cates Tom Fletcher Miriah Meyer Tolga Tasdizen	**General Electric Global Research** **Bill Lorenson, Site PI** Dan Blezek Jim Miller Xiaodong Tao
Massachusetts Institute of Technology (MIT) **Eric Grimson, Site PI** Polina Golland Lauren O'Donnell Wanmei Ou Kilian Pohl Lilla Zollei	**Kitware** **Will Schroeder, Kitware PI** Sebastien Barre Andy Cedilnik Luis Ibanez Karthik Krishnan Mathieu Malaterre
University of North Carolina (UNC) **Guido Gerig, Site PI** Isabelle Corouge Stasey Goodlett Ipek Oguz Martin Styner	**Isomics** **Steve Pieper, Isomics, PI** Alex Yarmakovich
Georgia Institute of Technology (GATech) **Allen Tannenbaum, Site PI** Ramsey Al-Hakim Shawn Lankton Xavier LeFaucheru James Malcolm Oleg Michailovich John Melonakos Delphine Nain Eric Pichon Yogesh Rathi Tauseef ur REhman	**UCLA** **Art Toga, Site PI** Ivo Dinov Michael Pan Jagadeeswaran Rajendiran
Massachusetts General Hospital (MGH) **Dave Kennedy, Site PI** Bruce Fishl Dennis Jen David Tuch Josh Snyder	**UCSD** **Mark Ellisman, Site PI** Brendan Flaherty Jeff Grethe
Isomics **Steve Pieper, Site PI** Alex Yarmakovich	

Appendix B (cont)

CORE 3: DRIVING BIOLOGIC PROBLEMS

DBP 1: Harvard-BWH-PNL
Martha Shenton, Site PI
Sylvain Bouix
Mark Dreusicke
Min-Seong Koo
Marek Kubicki
Jim Levitt
Motoaki Nakamura
Marc Neithammer
Katarina Quintos

DBP 2: Dartmouth
Andy Saykin, Site PI
Laura Flashman
Stephen Guerin
Alan Green
Nancy Koven
Thomas McAllister
John MacDonald
Tara McHugh
Heather Pixley
JD Pendergrass
Bob Roth
John West

DBP 3: UCI
Steve Potkin, Site PI
James Fallon
Diane Highum
Yi Jin
Lisa Kilpatrick
David Medina
Martina Panzenboeck
Padhraic Smyth
Hal Stern
Liv Trondsen
Jessica Turner

Toronto
Jim Kennedy, Co PI
Fabio Macciardi
Aristotole Voineskos

Harvard-BWH-SPL
Stephen Wong, Site PI
Nicole Aucoin
Steve Haker
Mike Halle
Katie Hayes
Raul San Jose
Gordon Kindlmann
Haihing Liu
Doug Markant
Wendy Plesniak
Sonya Pujol
Carsten Richter
Sandy Wells
Carl-Fredrik Weston
Cindy Wible

CORE 4: SERVICE
WILL SCHROEDER, CORE PI
Kitware, Inc.
Will Schroeder, Core PI
Andy Cedilnik

CORE 5: TRAINING
Randy Gollub, Core PI
Harvard-MGH
Guido Gerig, Site PI
UNC
Ross Whitaker, Site PI
Utah
Martha Shenton, Site PI
Harvard-BWH-PNL
Sonia Pujol, Harvard-BWH-SPL

CORE 6: DISSEMINATION
Steve Pieper, Isomics, CO-PI
Tina Kapur, Epiphany Medical, CO-PI

CORE 7: LEADERSHIP
Ron Kikinis, Core PI
Steve Wong