National Alliance for Medical Image Computing (NAMIC)

Core 1: Computational Foundations

A. Specific Aims:

As described in the original proposal, the aims of Core 1 are to create, develop, integrate and deploy computation tools for the analysis and visualization of medical image data. These computational tools are specifically focused on issues related to the driving biological problems posed by the study of schizophrenia. Consistent with these aims, work on computational methods during the first year has focused on:

- Definition of anatomical structures, at varying scales and levels of distinctiveness;
- Measurements of properties of extracted structures;
- Connectivity and systems analysis.

B. Studies and Results

Algorithm development for extracting model of anatomical structures has focused on two different classes of algorithms. Both use shape information to guide the segmentation of new scans: one is based on evolving boundaries of structures to fit image data, while incorporating prior knowledge about standard shapes of structures; the other is based on statistical assignment of tissue labels to voxels, while being influenced by prior knowledge about shapes of structures and their relative layout. Both classes of algorithms have been designed, implemented, tested and are being inserted into the NAMIC toolkit for use by other researchers.

Algorithm development for measurements of properties of anatomical structures has focused on shape measurements associated with segmented structures. We have developed mathematical modeling approaches to comparing populations based on the shape of anatomical structures. In contrast with shape-based segmentation that utilizes a statistical model of the shape variability in one population (typically based on the Principal Component Analysis) we are interested in identifying and characterizing differences between two sets of shape examples. We use a discriminative framework to characterize the differences in shape by training a classifier function and studying its sensitivity to small perturbations in the input data. Additional algorithmic methods have been incorporated for performing group-level statistical analysis of DTI data in a number of clinical applications.

In complementary work, we have developed novel methods in shape analysis for a) the computation of local thickness maps at the surface using Voronoi skeletons and b) the parcellation of 2D and 3D boundary shape descriptions in order to measure regional effects of volume, area, shape and diffusion tensor properties. The statistical local shape analysis methods were extended to incorporate multivariate Hotelling T^2 size and significance maps, both raw and corrected for multiple comparison, as well as effect size and regression coefficient r^2 maps. These additional maps are crucial in the correct validation and interpretation of local shape statistics.

We have also developed a novel algorithm that learns the shape variation at multiple scales and locations based on a training set. Our technique uses spherical wavelets to generate a multiresolution description of surfaces and spectral graph partitioning to adaptively discover independent shape variations at multiple scales. Our results show that our algorithm significantly improves the approximation of shapes in a testing set over PCA that tends to oversmooth the data.

In addition to creating algorithmic methods for measuring properties of structural elements, we have also been creating and deploying tools for measuring properties of white matter tracts. Whereas tractography on DTI is mostly used to study the white matter architecture, we extend this concept towards quantitative tractography. The development augments white matter bundle extraction by a set of methods that provide diffusion tensor analysis for individual tracts. The tool includes clustering of sets of streamlines into coherent bundles with outlier removal, interpolation of sets of curves by B-splines and arc-length parameterization, calculation of diffusion statistics in cross-sections and along bundles, and standardized output of statistics into files. User interaction is facilitated by a graphical user interface with fiber bundle editing and visualization options.

Algorithm development for connectivity analysis has focused on methods for analyzing and visualization DTI data. In particular, we are developing algorithms that measure connectivity of white matter using geodesic flow information, and that measure connectivity by directly tracking local orientation preferences at voxels. Secondly, we are developing algorithms for clustering tensor information into coherent bundles. Visualization methods have been incorporated into the NAMIC toolkit, which enable a user to view these bundles and their clusters, both within a patient and across sets of patients. These include tract based visualization tools, as well as tools for visualization of high angular resolution diffusion imaging data.

C. **Significance**

The primary goal of Core 1 is to develop algorithms that can be used by Core 3 (and other) collaborators to investigate questions about the development, and impact, of schizophrenia, as well as other diseases. The newly developed segmentation algorithms have been demonstrated to provide more accurate reconstructions of anatomical structures, leading to more detailed and refined analysis of differences in structure between normal and diseased subject populations. The standardization efforts in shape analysis will facilitate the development of tools incorporating methods from different NAMIC sites. Such tools designed for clinical study partners are currently non-existent in the shape analysis field. These new standardized tools will provide a significant impact on the measurement and comparison of shape populations.

The methods developed for parcellation and thickness analysis further strengthen shape analysis based studies and showed great potential in our initial analysis applied to the hippocampus and the corpus callosum. We expect these tools to further support the quantitative study of structures implicated by schizophrenia. The related tools developed for visualization of white matter tracts, and for clustering of tracts both within a subject and across subjects, are already being used by collaborators investigating questions in schizophrenia analysis.

D. **Plans**

Consistent with our original goals, the second year of NAMIC will focus on continued integration of algorithmic tools into a framework that is easily accessible to clinical researchers. The testing of the integrated framework on clinical data (already underway in a number of collaborations between Core 1 and Core 3 sites) will provide valuable feedback to the algorithm developers in creating the next generation of methods. Focus will again be divided between DTI processing and analysis, structure analysis, and shape population studies and comparisons.