Biomedical Informatics Research Network: Integrating Multi-Site Neuroimaging Data Acquisition, Data Sharing and Brain Morphometric Processing

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Abstract

The Biomedical Informatics Research Network (BIRN) is a National Institutes of Health (USA) initiative that fosters distributed collaborations in biomedical science by utilizing information technology innovations. Morphometry BIRN is one of its testbeds and has the goal to develop the ability to conduct clinical imaging studies across multiple sites, to analyze structural imaging data with the most powerful software regardless of development site, and to test new hypotheses on large collections of subjects with well-characterized image and clinical data. Through large-scale analyses of patient population data acquired and pooled across sites, we are investigating neuroanatomic correlates of Alzheimer's Disease Depression and Mild Cognitive Impairment subjects. This paper describes progress in multi-site image calibration and in software integration for multi-site image processing.

1. Introduction

The Biomedical Information Research Network (BIRN, www.nbirn.net) is a National Institute of Health consortium in the USA comprised of 26 research groups that aims to create technical infrastructure and guidelines to enable acquisition, databasing, sharing, analysis and mining of multi-institutional biomedical data [1]. In it's first phase BIRN is focused on clinical neuroscience through the coordinated work of the following testbeds: Functional Imaging Research in Schizophrenia Testbed BIRN (integration and analysis of functional MRI data), Mouse BIRN (integration of multi-scale neuroimaging and genetic data from mouse models of neurological and psychiatric disorders), BIRN Coordinating Center (support

for network infrastructure, grid computing, data integration, interaction environments and general coordination of the project), and Brain Morphometry BIRN (discussed in this paper).

The Morphometry BIRN's goal is to develop the ability to conduct clinical imaging studies across multiple sites, to analyze imaging data with the most powerful software regardless of development site, and to test new hypotheses on large collections of subjects with well characterized image and clinical data. Through large-scale analyses of patient population data acquired and pooled across sites, we are investigating neuroanatomic correlates of Alzheimer's Disease, Depression and Mild Cognitive Impairment subjects. Currently, the Morphometry BIRN sites are: Massachusetts General Hospital (MGH, lead site), Brigham & Women's Hospital (BWH), Johns Hopkins University (JHU), Washington University in St. Louis (WashU), Massachusetts Institute of Technology (MIT), Duke University, University of California San Diego (UCSD), Los Angeles (UCLA) and Irvine (UCI).

Challenges of the BIRN effort include calibrating imaging data acquired from multiple sites and integrating software analysis and visualization tools developed at different sites. In this paper we summarize results of work on these fronts.

2. Multi-Site Structural MRI Calibration: gradient-distortion correction

2.1. Introduction

One of the challenges of both multi-site and longitudinal neuroimaging studies is to maximize MR image reproducibility over time. In other words, to minimize technology related variability in the images, which limits the power for following the progression of disease and finding biomarkers. This motivates the development and application of procedures both to standardize acquisition parameters and to estimate and correct for the error introduced by uncontrolled factors, particularly when data from multiple scanners and MRI vendors are combined. An important task in this effort is to accurately correct for gradient-induced distortions in order to allow cross-site comparisons of morphometry results, minimizing dependence on site-specific factors. Here we present results from a phantom and human study that shows how image reproducibility can be significantly improved when with gradient distortion correction. To keep our results independent of brain morphometry tools, here we focus only on the reproducibility of image intensity for the human data

2.2 Materials and Methods

To quantitatively characterize the extent of image distortions due to gradient non-linearities, phantom and test-retest human data were collected from multiple sites having different commercial 1.5T whole body scanners used for functional and structural MRI studies: General Electric Signa CVi/NVi 1.5T at Duke and BWH (CRM gradients with max strength, slew rate = 40mT/m, 150T/m/s), the same vendor but different gradients for UCSD (22mT/m, 120mT/m/ms), and Siemens Medical Systems Magnetom Sonata 1.5T from MGH (Sonata gradients, 40mT/m, 200T/m/s). T1-weighted structural MRI data used for morphometry were acquired [2]. The distortion correction consisted of two steps. First, a displacement vector map was calculated using the spherical harmonic coefficients from the vendor's true gradients. Second, the displacement and intensity correction maps were applied to the original image.

2.3. Results

Figure 2.1 summarizes the group results for the phantom scans across the 4 sites (MGH, BWH, Duke and UCSD), showing how the multi-site diameter errors (measured diameter relative to true diameter) are significantly reduced after distortion correction ($p<0.001$). At the phantom edges the uncorrected diameter errors were about (5+-2)%, whereas for the corrected images the deviation from the true diameter was (0.5+-0.08)%. The human results (Fig. 2.2) showed that image intensity fluctuations arising from voxel distortions can be signifcantly reduced both in within-site (10% reduction in mean error) and across-site (16% reduction) comparisons.

2.4. Conclusions

The multi-site phantom results validated the gradient distortion correction method, showing that the geometric distortions of a phantom can be significantly reduced. The test-retest human data, within- and across-site results, showed that image intensity reproducibility is significantly improved with distortion correction. As expected, the correction effects are strongest in across-site comparisons. This is consistent with the fact that in multi-site scanning the variability in subject's positioning is added to the variability in distortion fields from the different sites. We also found that the differences in within-site reproducibility errors between the sites could be explained by reproducibility errors in the positioning of the subjects. In conclusion, correction for gradient non-linearity errors has the potential for improving the accuracy of morphometric analysis in longitudinal and multi-site imaging studies. These corrections, however, do not account for all the sources of image intensity variability, which are likely to include inhomogeneities of the B_1 RF pulses.

3. Developing a shape analysis processing pipeline

3.1. Introduction

Brain morphometric analysis and visualization tools from multiple sites are being integrated to operate together on data acquired at different sites. The goal is to develop a uniform platform that will enable clinical scientists to seamlessly access, visualize, process and store imaging and clinical data, as well as analyses results. To drive such developments we started with focused efforts. One of them, which we describe here, is the development of a shape analysis pipeline that can enable pattern classification of hippocampal shape for research in Alzheimer's Disease. In this example, imaging data acquired at one site (WashU) is analyzed by integrated morphometry tools from two other different sites (MGH and JHU), and a visualization tool from a fourth site (BWH) has been extended to enable the viewing of all the derived results on a single visualization platform.

3.2. Materials and Methods

Figure 3.1 shows a schematic representation of the data flow in the shape analysis pipeline. 45 subjects (21 nondemented controls, 18 very mild Alzheimer's Disease, 6 semantic dementia) were scanned using high resolution T1-weighted structural MRI at Washington University in Saint Louis. Then the anonymized scans were analyzed at MGH's Martinos Center using Freesurfer [3]. The resulting segmented data sets were aligned and processed at JHU's Center for Imaging Science (CIS) using the Large Deformation Diffeomorphic Metric Mapping (LDDMM) tool [4]. Briefly, LDDMM computes the diffeomorphic transformation of one binary image *I0* to another *I1* along with the metric distance between them generated

by the geodesic connection between the images through the group of infinite dimensional diffeomorphisms (which is the generalization of rotations, translations and scale group), the necessary group for studying shape.

TeraGrid resources were used for the LDDMM computations. Clusters of 70 concurrent LDDMM processes were running for 8 hours each on nodes of the TeraGrid.

From the 4050 LDDMM comparisons of left and right hippocampal shapes, a statistical analysis of the two-45x45 matrix of metric distances was done. First, these distances were non-linearly mapped to *Rd* space by a multidimensional scaling (MDS) [5] to minimize the inter-point distance distortion in Euclidean space. The classical MDS produced a *dL+dR* dimensional feature matrix, which was used to perform classification via linear discriminant analysis (LDA) [6]. The performance criteria of the classification measures the instances of misclassification with leave-one-out cross validation.

3.3. Results

Integration code developed at MGH, JHU and BWH facilitated the exchange and visualization of morphometric results (subcortical segmentations and shape vector fields). Figure 3.2 shows a 2D scatter plot generated by LDA. As it can be seen, class-specific information (subject diagnosis) can be extracted from the shape analysis results performed by LDDMM on hippocampus shapes that were previously segmented by Freesurfer.

3.4. Conclusions

The extensibility of Freesurfer and LDDMM morphometric tools to operate seamlessly on data that was acquired at neither the MGH nor the JHU sites is noteworthy. Pattern classification of metric distances provides a powerful means of distinguishing shapes and providing the neuroanatomist an increased understanding of diseases and disorders with greater statistical power.

4. References

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5. Acknowledgements

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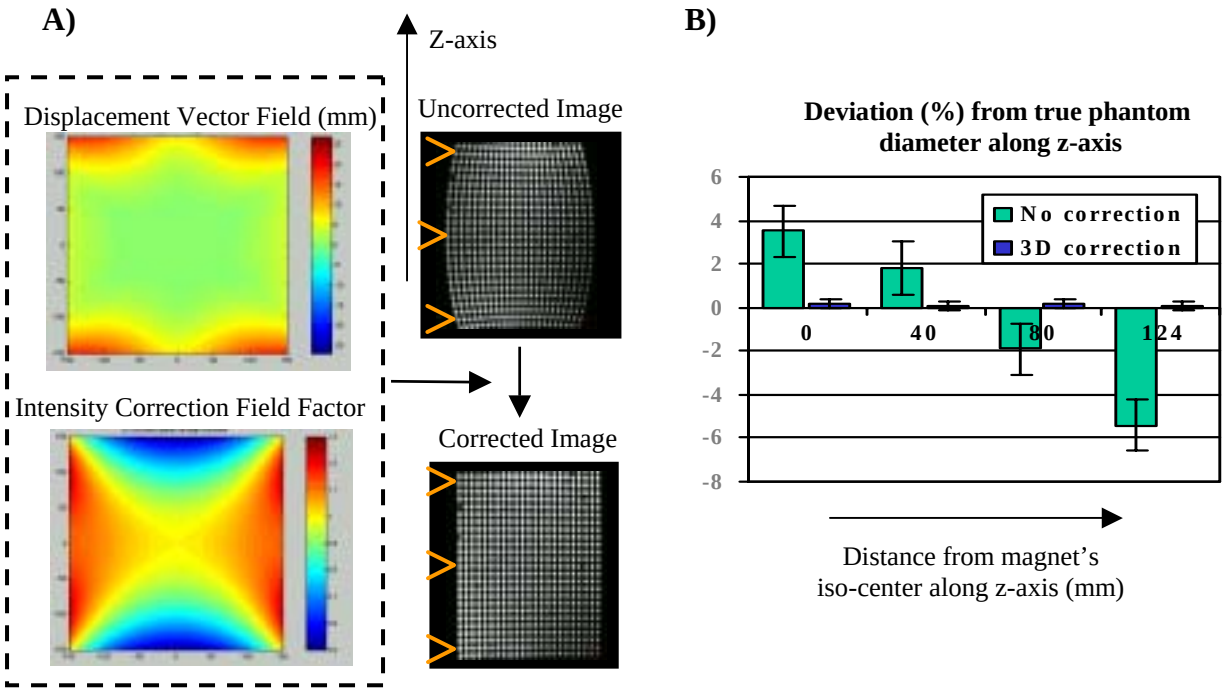

Figure 2.1: Phantom results. A) Schematic representation of the distortion correction process. B) Relative errors in phantom diameter measures (image measure divided true diameter) from MGH, BWH, Duke and UCSD sites, with (blue) and without (green) gradient distortion correction, as a function of the distance from magnet's iso-center along the z-axis (mm). The correction improves geometric reproducibility and accuracy.

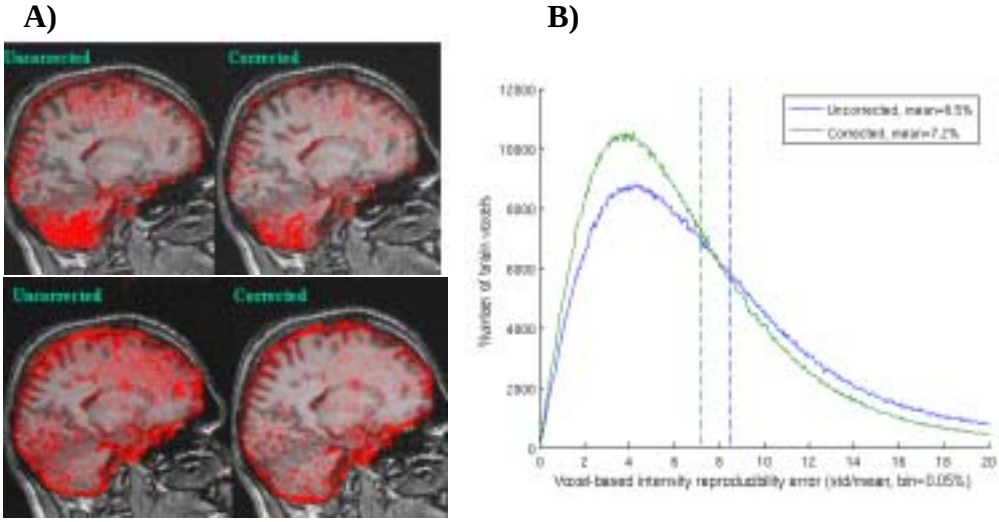

Figure 2.2: Distortion correction effects on image intensity reproducibility of human structural data. A) Voxel-based variability maps (standard deviation divided by the voxel mean), for a single subject test-retest within site (top, two sessions) and the same subject test-retest across sites (bottom, three sessions). Intensity variations larger than 8% are shown in red overlaid on one of the subject's structural scan. B) Distortion correction effects on the histograms of the across-site variability maps. Mean reproducibility errors of image intensity are significantly reduced.

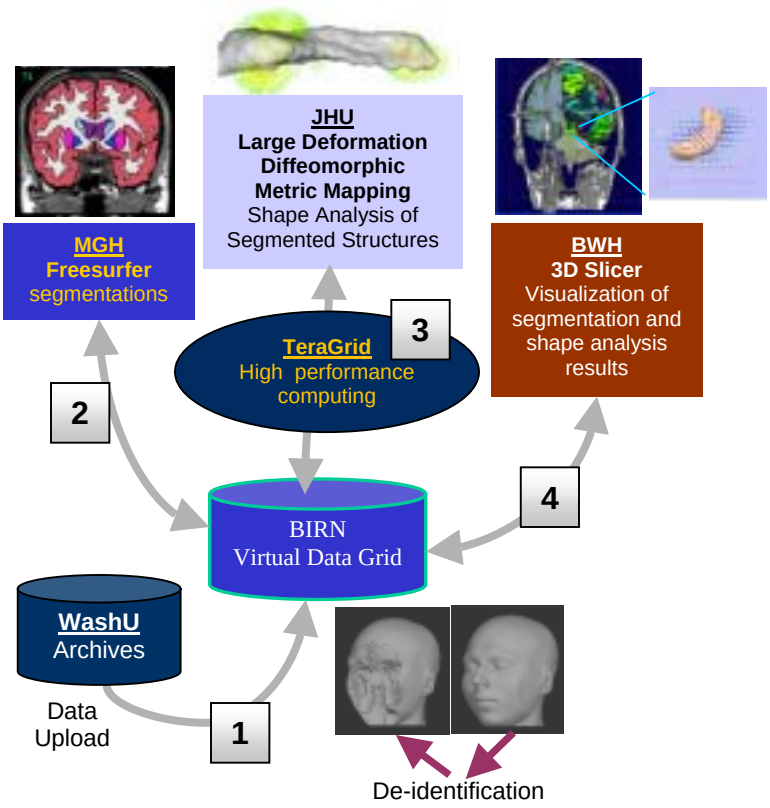

Figure 3.1: Dataflow for the shape analysis-processing pipeline. 1) Structural MRI data upload from WashU 2) Semi-automated subcortical segmentation (MGH). 3) Shape analyses of segmented hippocampus data (JHU). 4) Visualization of combined morphometric results (BWH).

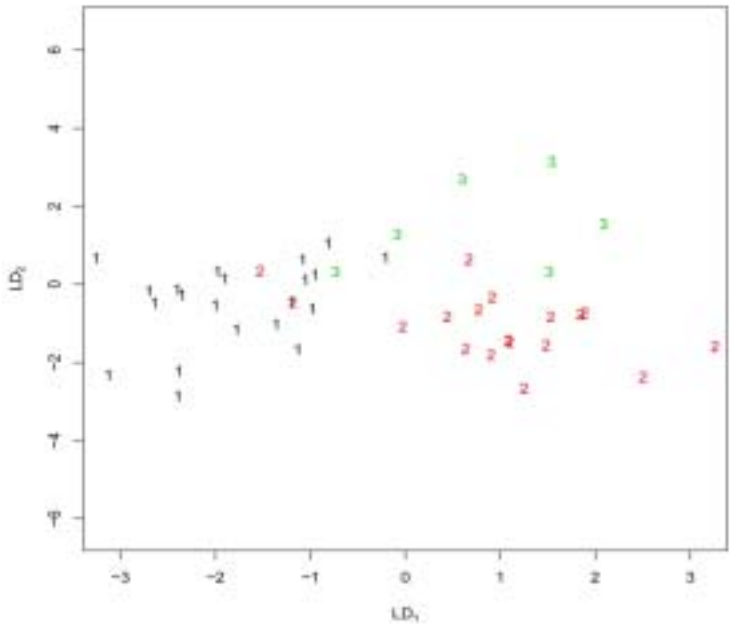

Figure 3.2: 2D scatter plot generated by LDA. Class labels are represented by Non-demented Controls (1), Alzheimer's Disease (2) and Semantic Dementia (3)