



## Neuroscience Research Services

Neuromorphometrics provides brain measurement services. Given raw MRI brain scans, we make precise quantitative measurements of the volume, shape, and location of specific neuroanatomical structures. The final measurements result from automated analyses that are manually guided, inspected and certified by a neuroanatomical expert. More than two months of training are required for this person to be able to identify and delineate the borders of the structures on each slice where they appear. All data from raw images through final results are checked for completeness and integrity. The validity of the results is assured by reporting on inter- and intra-observer repeatability measures.

### *Typical Study*

#### **Anatomical Analysis**

We currently have well-defined and robust methods for measuring the: cerebral exteriors, cerebellum exteriors, lateral ventricle, inferior lateral ventricle, third ventricle, fourth ventricle, optic chiasm, brainstem, caudate, putamen, pallidum, nucleus accumbens, thalamus, hippocampus, amygdala, cerebral white matter, cerebellum white matter, cerebellar vermal lobules (I-V, VI-VII, VIII-X), and also a parcellation of the cortex and white matter into: insula, frontal, parietal, occipital, and temporal lobes. We continually work with customers to refine existing measurement methods and to develop and apply new ones, and we will work with you to apply any measurement protocol that is available.

#### **Personnel**

Each study involves various people as needed: image processing expert, MR imaging consultant, neurologist or neuroradiologist, anatomist, technician, computer system administrator, and programmer.

#### **Combined Automated and Manual Methods**

Automated processes in the analysis pipeline include: bias field correction, intensity estimation, and neuroanatomical labeling. The strengths of the automation come from using anatomical information from both a probabilistic atlas of previous segmented scans and also from ad hoc rules that have time tested reliability. Manual intervention is accomplished with “NVM”, open source software that we have developed in-house with support from SBIR grants from the NIH. This tool uses histograms, isointensity contours and the manual drawing and erasing of borders where necessary. Both object and source code for NVM are publicly available, and it runs on Linux, Windows and Macintosh computers.

#### **Assured Validation**

To demonstrate the validity of our results, multiple operators perform multiple blind analyses of the same scan, or preferably of same subject re-scanned multiple times. This allows us to

monitor our performance with inter- and intra-observer statistics. In addition, each and every measurement is run through automated consistency and “sanity” checks, and also inspected visually by an anatomist.

## **Data integrity and security**

The integrity of all images, accompanying data and analysis results are demonstrably maintained such that nothing is lost, inappropriately released, or corrupted. This is done using established procedures involving log files, digital signatures, checksums, continual consistency and completeness inspections for raw data and results, and redundant archiving.

Initially received data is inspected to be sure it is complete, uncorrupted and appropriate for the following analyses. This is done using automated checks for the presence and sizes of files and by visual image quality examinations. Once in the analysis pipeline, calculating and matching checksums confirms data file integrity. Actual results are matched with expected outcomes whenever possible by using, for example, range checks on measurements, or by making sure that sub-volumes add up to their total volume. In addition to all data, all documentation and software is also archived. Data and log files are digitally signed and encrypted (if necessary) to insure accountability, integrity, and security.

## **SegMentor Scripts: Accountability in Methodology and Analysis**

Neuroanatomical measurement results are difficult to reproduce when they are incompletely defined or improperly executed. This can be the case when applying methods that are described in academic publications because there is not enough room to present comprehensive details along with results. Moreover, slight differences in the interpretation of the definition of an anatomical boundary or differences in the perception of how that boundary appears in a MRI slice can significantly alter the final measurement. To demonstrate the accountability of a neuroanatomical measurement method, it must be comprehensively documented in addition to being accurately conveyed and executed.

“SegMentor” is the name of the feature in our analysis software that addresses this problem. Its purpose is to explicitly define and embed neuroanatomical measurement methods into the software. It tightly couples the measurement method to the tool by providing 1) short on-line, context-sensitive text instructions, 2) hyperlinks to web pages containing detailed anatomical border definitions, and 3) actively assists with segmentation by controlling the software. SegMentor records, plays, and allows viewing and editing of scripts that provide information to the user and also control the rest of the program. It also allows images and text to be captured as web pages to document segmentation procedures.

SegMentor increases the reliability and repeatability of measurements because it enforces and documents particular sequences of analysis procedures to insure that a prescribed measurement method is followed.

## **Raw Data**

Neuromorphometrics typically uses MRI brain scans that are T1-weighted, contiguous coronal slices with 1mm in-plane resolution and 5mm slice thickness (120 slices). We can adapt our analysis procedures to T2-PD weighted scans and other types of data.

## ***Project Timeline***

### **Initial Setup**

- Determine/disseminate scanning protocols as necessary
- Develop/Modify anatomical procedures
- Develop/Modify image processing (automation) procedures
- Train technician on specific procedures
- Set up and configure any necessary (locally and at customer site):
  - Software: NVM
  - Hardware: Computers, routers
  - Data transfer procedures: Using a VPN, sftp, or mailed tapes, CDs or DVDs.
- Deliver initial report describing scanning, image processing, and anatomical methods (SegMentor script)

### **Initial Study: check % of scans**

- Check data transfer and archiving procedures, scanning protocol, and image quality
- Evaluate image processing (automation)
- Measure scans
- Evaluate anatomical procedures by checking technician's results.
- Modify all procedures and methods as necessary to get sufficient precisions and reproducibility.
- Deliver report describing scanning, image processing, and anatomical methods (SegMentor script) that will be fixed for the main study.

### **Main Study**

- Transfer and archive data, check image quality
- Run image processing (automation)
- Measure scans
- Anatomically review all results

### **Final Report**

- Deliver results and validation statistics: volumes, outlines
- Deliver final project documentation (SegMentor script) indicating any changes.

## **Why Use Our Services?**

Neuromorphometrics emphasizes precise and specific measurements of individual neuroanatomical structures. This is beyond just measuring gray matter, white matter and CSF regions and provides more information than measurements made on averaged brain scans. Since our anatomists have been trained at the MGH CMA, we use established methods, but we can also adapt them for a specific project and create new methods. We can efficiently and reproducibly measure large numbers of subjects, and we can deliver results on a reliable schedule. We save customers time and also some of the costs of an equivalent analysis because we take care of establishing procedures, setting up equipment and training anatomists.