

The following paragraphs describe the methods that were used on the different version(s) of the Alzheimer's Disease Template.

## Alzheimer's Disease Template

Corrected 2015

The AD Atlas is a population-based, disease-specific brain atlas that reflects the unique anatomy and physiology of this particular clinical subpopulation. It was constructed, to represent the human brain in Alzheimer's Disease (AD). To quantify patterns of anatomic variability in a relatively large, homogeneous group of subjects, a reference image archive was constructed from high-resolution 3D (2562x124) T1-weighted fast SPGR (spoiled GRASS) MRI volumes, acquired from 26 subjects diagnosed with mild to moderate Alzheimer's Disease (AD; NINCDS-ADRDA criteria). All subjects were matched for age (75.8-1.7 yrs.; 14 females/12 males), educational level (15.2-0.4 yrs.), disease severity, and handedness (all right-handed). The patient group had a mean Mini- Mental State Exam score of 20.0-0.8 (maximum score: 30, Folstein et al., 1975). Scan acquisition parameters were TR/TE 14.3/3.2 msec, flip angle 35°, NEX=1, FOV 25cm, with contiguous 1.5-mm thick slices (no interslice gap) covering the entire brain.

Specialized strategies were developed to create a population-based average of the anatomy. Sets of high-dimensional elastic mappings, based on the principles of continuum mechanics, reconfigured the anatomy of a large number of subjects in an anatomic image database. These mappings generated a local encoding of anatomic variability, and were used to create a crisp anatomical image template with highly-resolved structures in their mean spatial location. Specialized approaches also were developed to average cortical topography. Since cortical patterns are altered in a variety of diseases, gyral pattern matching was used to encode the magnitude and principal directions of local cortical variation. In the resulting cortical templates, subtle features emerged. Regional asymmetries appeared that were not apparent in individual anatomies. The resulting atlas can identify patterns of altered structure and function, and can guide algorithms for knowledge-based image analysis, automated image labeling, tissue classification, data mining and functional.