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An image analysis and classification protocol for characterization of normal and abnormal aging via structural MRI

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Background: Early detection of structural brain changes that might be precursors to mild cognitive impairment (MCI) and Alzheimer's Disease must be distinguished from background normal aging affects, in order for structural analysis to be useful as an early diagnostic tool. **Methods:** We present a methodology for the quantitative analysis and classification of structural MR images, and its application to the Baltimore Longitudinal Study of Aging (BLSA), aiming at establishing extensive normative data of structural changes in the aging brain, and at determining quantitative imaging profiles of abnormal aging. This methodology is based on mass-preserving shape transformations applied in conjunction with a high-dimensional deformable registration method of very high accuracy. The methodology results in tissue density maps (primarily white and gray matter, as well as CSF), which quantify potentially complex patterns of brain atrophy. These tissue density maps are examined in conjunction with powerful nonlinear pattern recognition techniques, in a framework for multi-variate nonlinear classification. **Conclusions:** Application of this method to 158 images from the BLSA resulted in spatial maps of normal aging, which quantify the % rate of change of various brain regions, as well the variability across individuals. Moreover, our analysis demonstrates associations between patterns of atrophy and MCI clinical status in a small set of 12 MCI patients.