Analysis of Longitudinal Shape Variability via Subject Specific Growth Modeling

James Fishbaugh[a], Marcel Prastawa[a], Stanley Durrleman[b], Joseph Piven[c] for the IBIS Network*, Guido Gerig[a]

[a]Scientific Computing and Imaging Institute, University of Utah

[b]INRIA/ICM, Pitié Salpêtrière Hospital, Paris, France

[c]Carolina Institute for Developmental Disabilities, University of North Carolina

National Alliance for Medical Image Computing

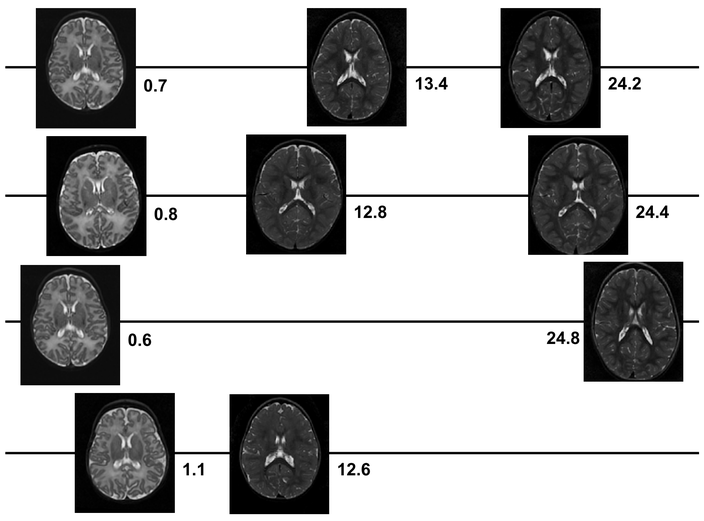
Introduction

Quantification of anatomical variability within a population and between populations are fundamental tasks in medical imaging studies. In many clinical applications, it is particularly crucial to quantify anatomical variability over time in order to determine disease progression and to isolate clinically important differences in both space and time. Methods have been proposed for the statistical analysis of cross-sectional time-series data, which do not contain repeated measurements of the same subject, such as [1]. In this work, we propose a new approach for analyzing statistical variability of shapes over time, in the spirit of [4,5], which is based on combining cross-sectional atlas construction with subject specific growth modeling.

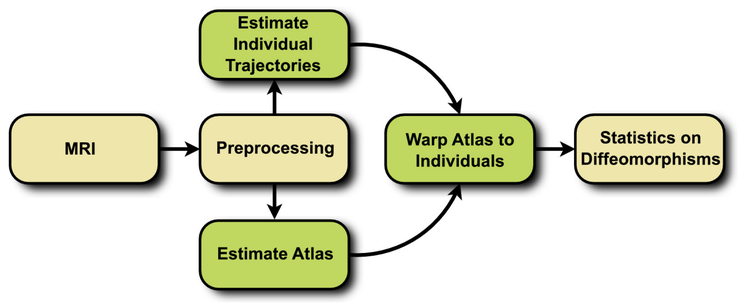
Methodology

Longitudinal Study Design

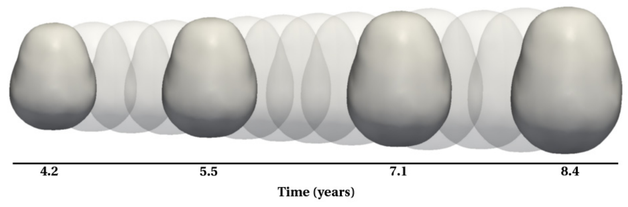
Longitudinal imaging data consists of repeated scans of the same subjects over time. Statistical analysis of longitudinal anatomical data is a problem with significant challenges due to the difficulty in modeling anatomical changes, such as growth, and comparing changes across different populations.



Processing Pipeline



The goal of **shape regression** is to infer a continuous evolution of shape from a discrete set of shapes S_{t_i} observed at time t_i.

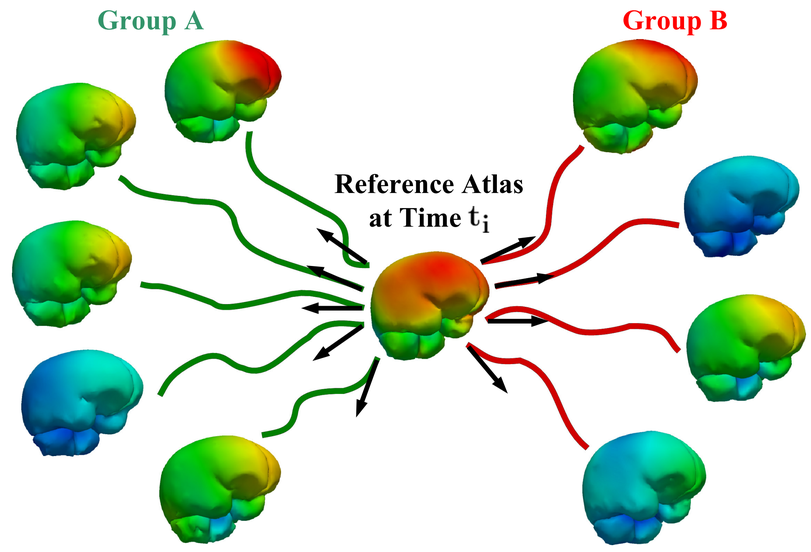


Using a temporally smooth acceleration controlled growth model [3], we build a 4D population atlas by estimating the average shape trajectory.

$$E = \sum_{t_i} d(\phi_{t_i}(S_0), S_{t_i})^2 + \gamma \mathrm{Reg}(\phi_t) \qquad \ddot{\phi}_t(x_i(t)) = a(x_i(t), t)$$

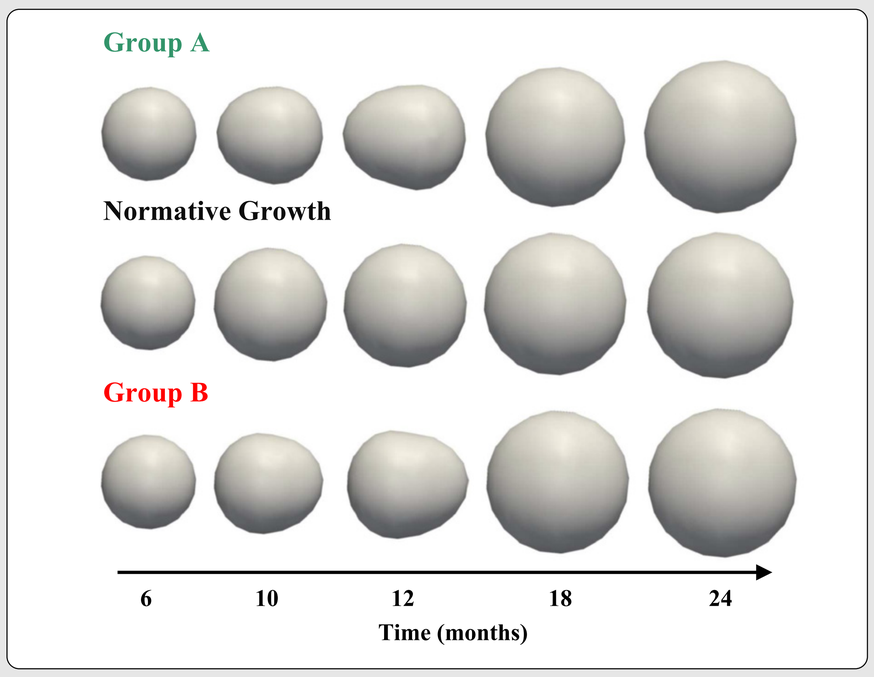
Analysis of Longitudinal Shape Variability

4D growth models are estimated for a reference population and independently for individuals in different groups. Statistics are conducted on initial momenta which parameterize geodesic flows of diffeomorphisms that match the reference atlas to each individual. Shape variability between groups with respect to the reference evolution can be investigated at any time point.



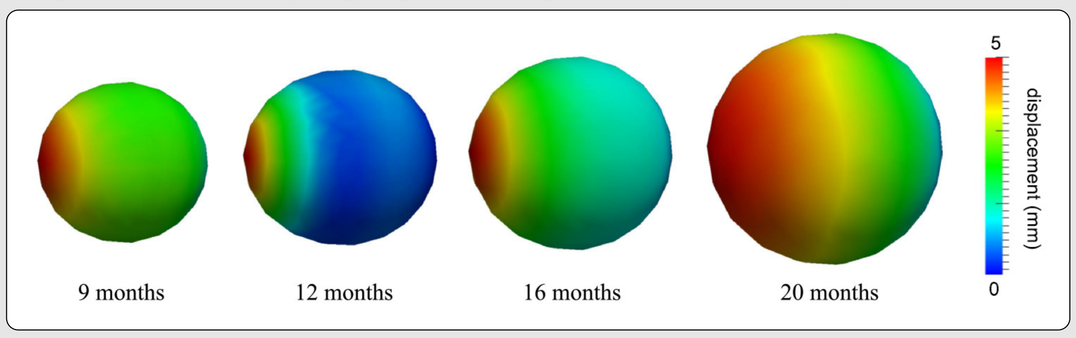
Experimental Validation

First, our framework is evaluated with a database of synthetic longitudinal shape data. We construct 12 subjects in each group by randomizing growth parameters.



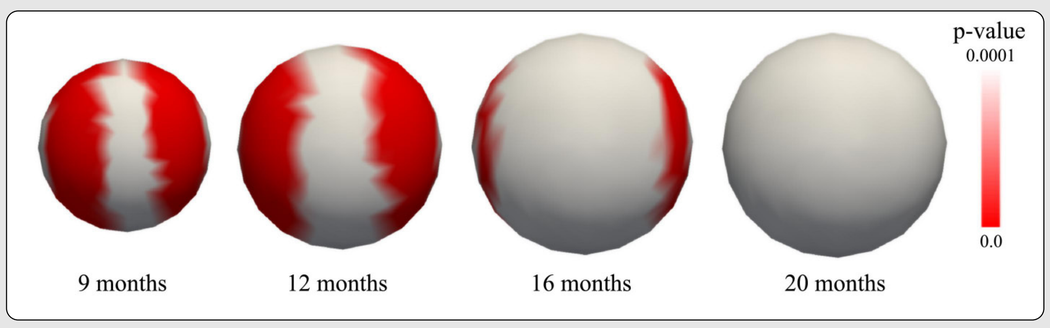
Shape Variability by Principal Component Analysis

Principal Component Analysis (PCA) on the momenta that warp the normative atlas to each individual in group A. The first major mode of variation is shown for several time points. This mode explains the variability in group A with respect to the reference shapes.



Hypothesis Testing for Group Differences

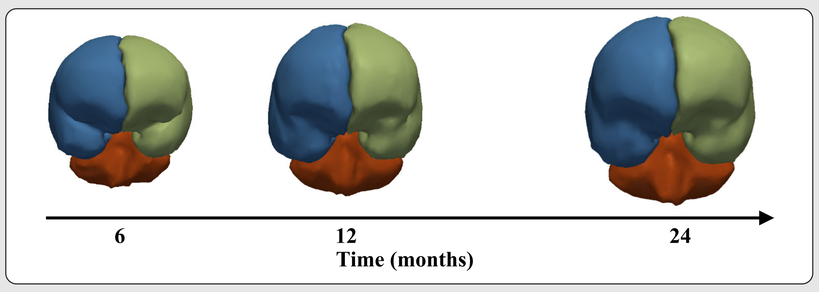
For each shape point an independent t-test is performed on the magnitude of initial momenta which match the reference atlas to individuals. The Bonferroni corrected p-values are shown on the reference atlas at selected time points.



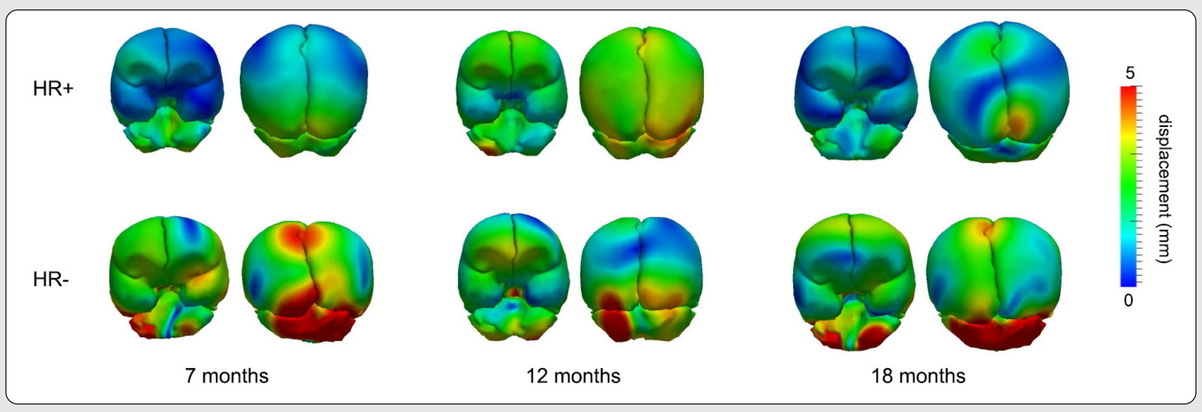
Clinical Application

The study consists of infants at high-risk for autism as well as controls, scanned at approximately 6, 12, and 24 months. At 24 months, symptoms of autism spectrum disorder (ASD) were measured using the Autism Diagnostic Observation Schedule (ADOS).

- **HR+**: 15 high-risk subjects with positive ADOS
- **HR-**: 40 high-risk subjects with negative ADOS
- **LR-**: 14 low risk controls with negative ADOS



PCA is conducted using the momenta vectors that parameterize the mapping from atlas to subject at each selected time point. The major modes of variability describe how each group varies from the normative growth scenario, shown for several time points of interest. Preliminary statistical testing did not reveal group differences in the left/right hemisphere or cerebellum.



Conclusion

We have proposed a new approach for analyzing shape variability over time, and for quantifying spatiotemporal population differences, combining:

- Atlas estimation
- Subject specific growth modeling

Future work will focus on:

- Leveraging longitudinal information in atlas construction, as in [2].
- Utilizing rate of change information, such as velocity/acceleration

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* The IBIS Network. Clinical Sites: University of North Carolina: J. Piven (IBIS Network PI), H.C. Hazlett, C. Chappell; University of Washington: S. Dager, A. Estes, D. Shaw; Washington University: K. Botteron, R. McKinstry, J. Constantino, J. Pruett; Childrens Hospital of Philadelphia: R. Schultz, S. Paterson; University of Alberta: L. Zwaigenbaum; Data Coordinating Center: Montreal Neurological Institute: A.C. Evans, D.L. Collins, G.B. Pike, P. Kostopoulos; Samir Das; Image Processing Core: University of Utah: G. Gerig; University of North Carolina: M. Styner; Statistical Analysis Core: University of North Carolina: H. Gu; Genetics Analysis Core: University of North Carolina: P. Sullivan, F. Wright.

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