NYU TANDON SCHOOL OF ENGINEERING

Studying Growth and Disease Trajectories from Longitudinal Imaging: Challenges and Opportunities

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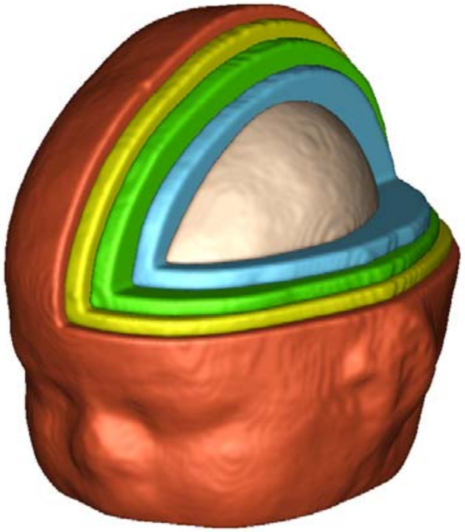
Computer Science & Engineering



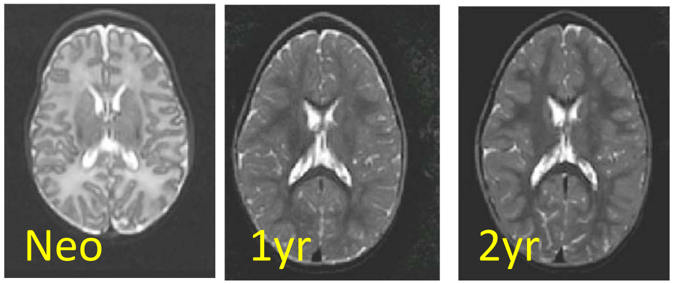
VIDA VISUALIZATION IMAGING AND DATA ANALYSIS CENTER

Computer Science and Engineering

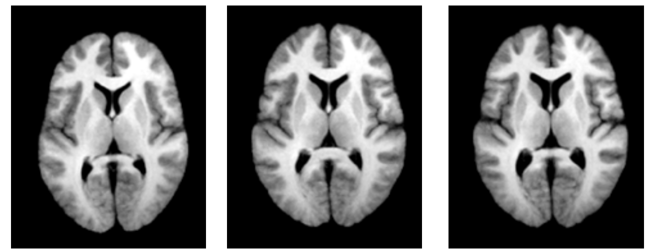
Contents

Longitudinal/Serial Image Data

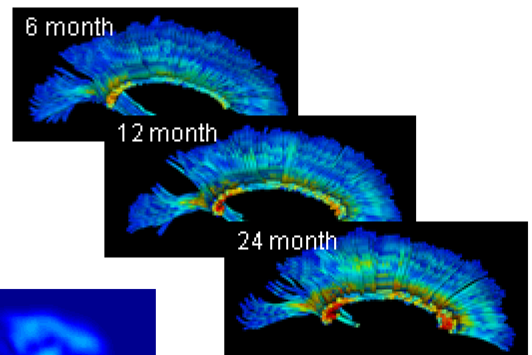
Pediatrics: Brain Growth



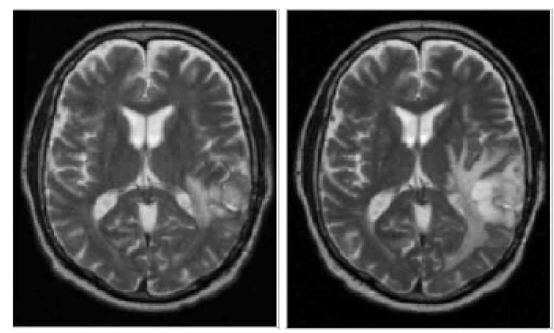
Aging / Neurodegeneration



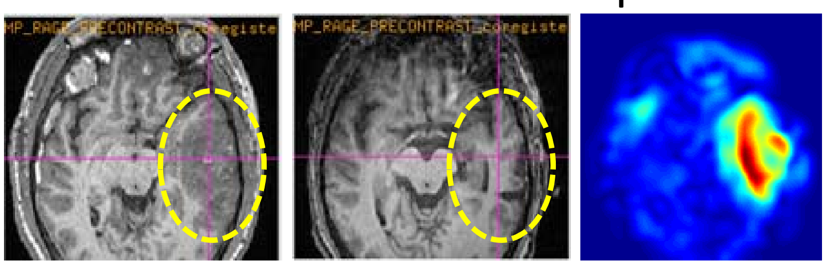
WM Maturation



Tumor Growth



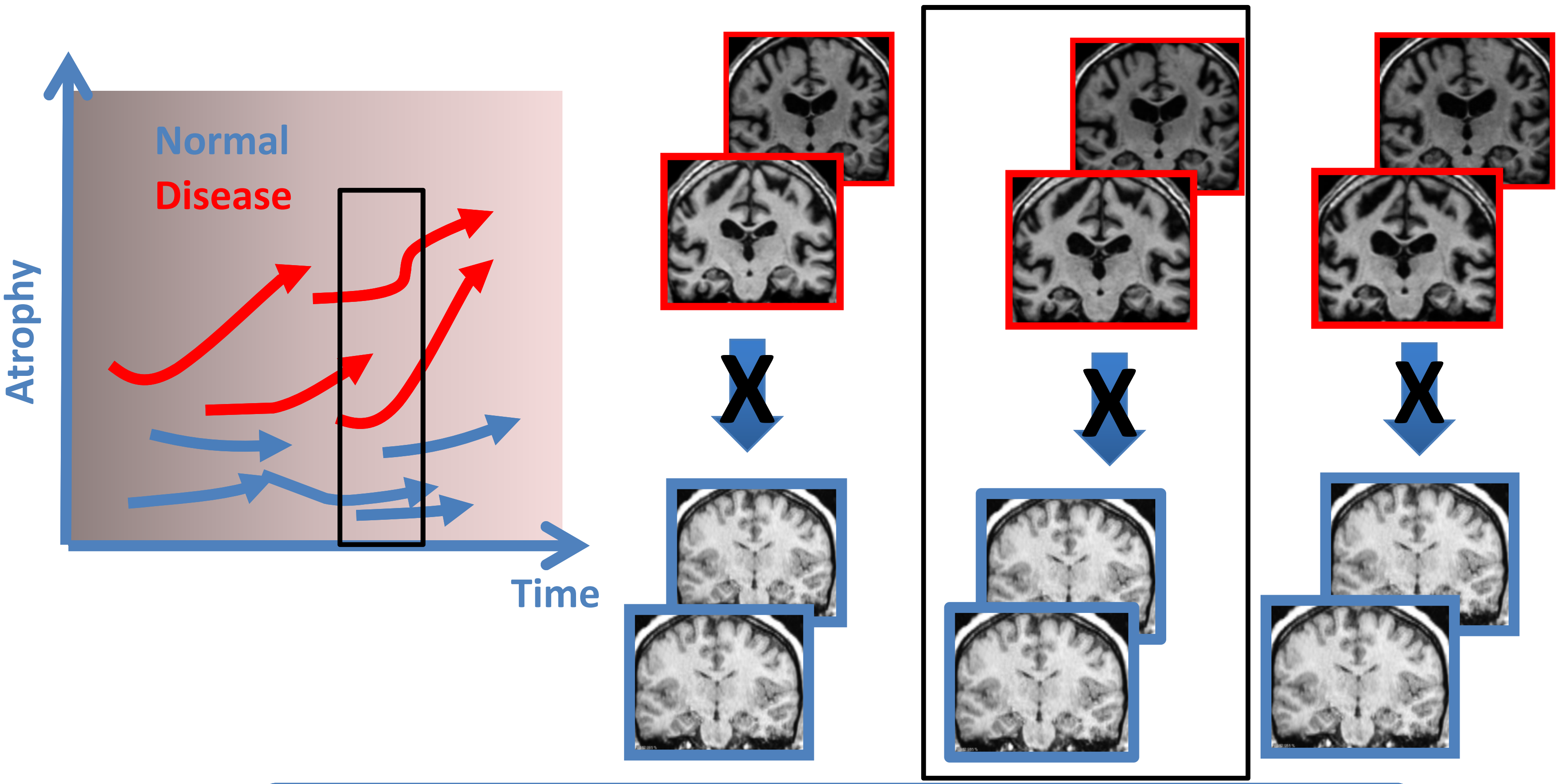
Trauma: Baseline – Follow-up



- Image analysis technology for 4-D data is lagging behind acquisition
- Often: individual time-point analysis, ignores causality of repeated imaging

Spatiotemporal Morphometry

Cross-sectional paradigm



Inter-subject variability >> Intra-subject changes

Courtesy of Lorenzi & Pennec, INRIA

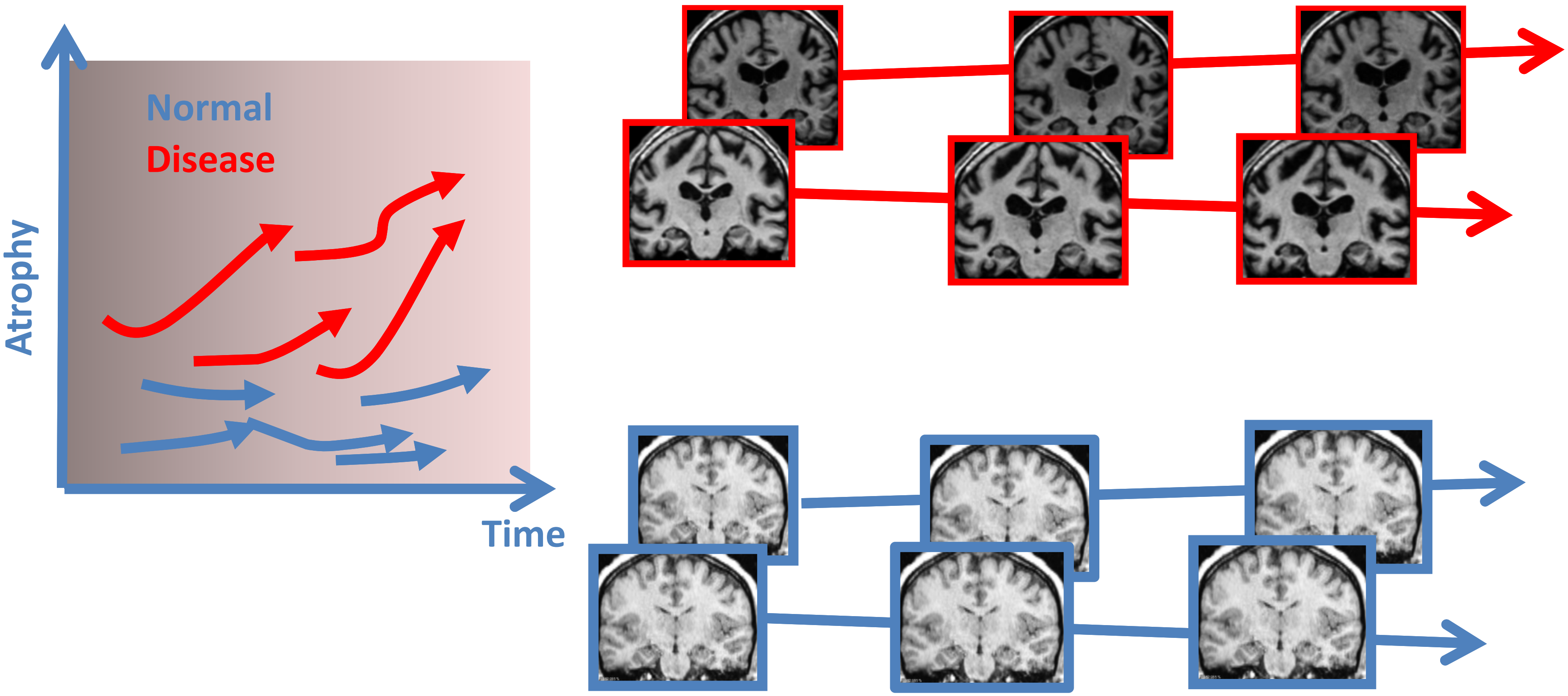
Spatiotemporal Modeling: Natural Task in Clinical Reasoning

- **Motivation**:
  - Development, degeneration, effects of therapeutic intervention are dynamic processes.
  - Personalized health care: Individual trajectories compared to expected “norm”.
  - Clinical terminology: Atypical, Monitoring
    - Departure from typical development, deviation from healthy
    - Typical but delayed growth patterns, catch-up, atypical development
    - Analysis of recovery for each patient
    - Predict onset of clinical symptoms, or pathological progression
    - Monitor efficacy of treatment

- → **Focus on longitudinal design & longitudinal analysis**

Spatiotemporal Morphometry

Longitudinal paradigm



Subject-specific Trajectories -> Group Testing on Trajectories

courtesy of Lorenzi & Pennec, INRIA

Regression

Fit a continuous model given discrete measurements

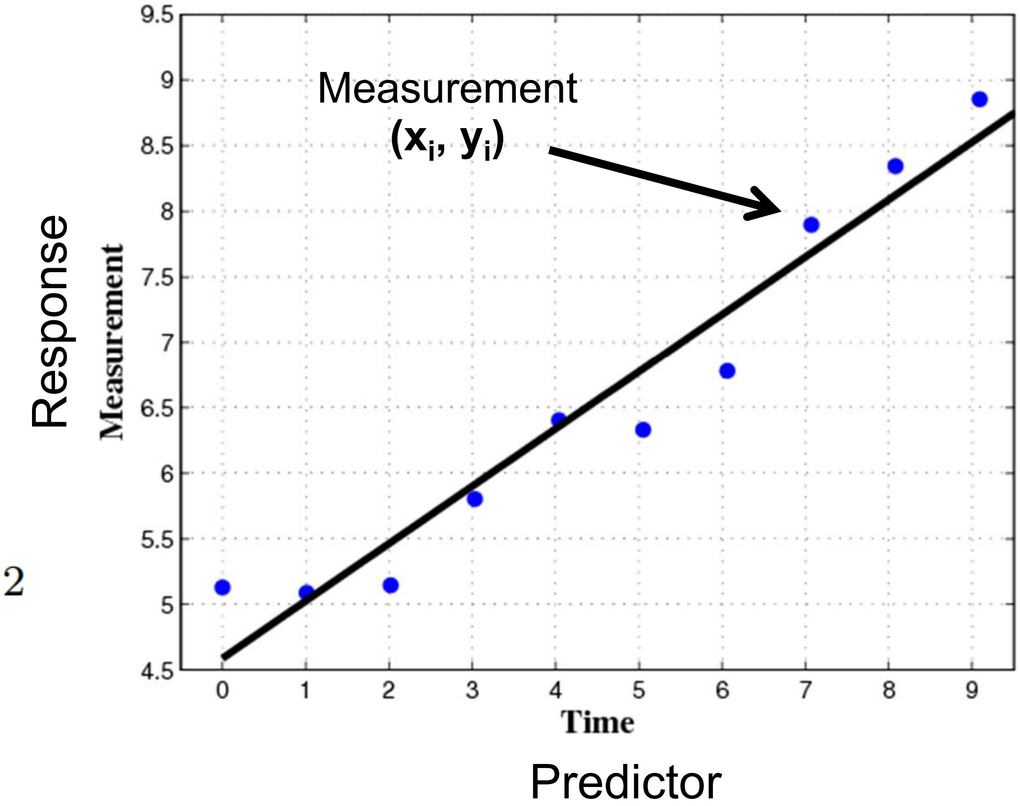
Simple linear regression:

$$y = \boxed{m}x + \boxed{b}$$

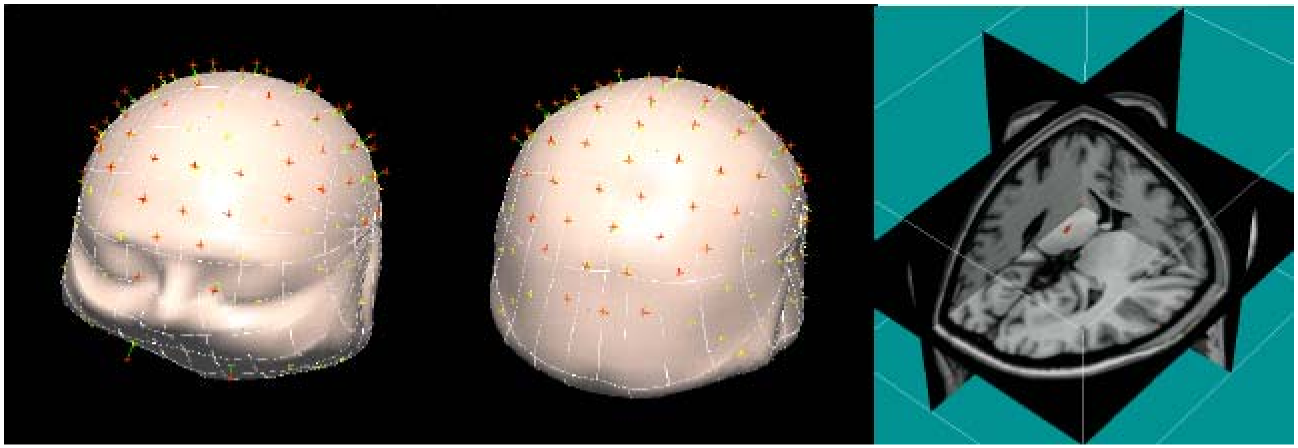
slope **intercept**

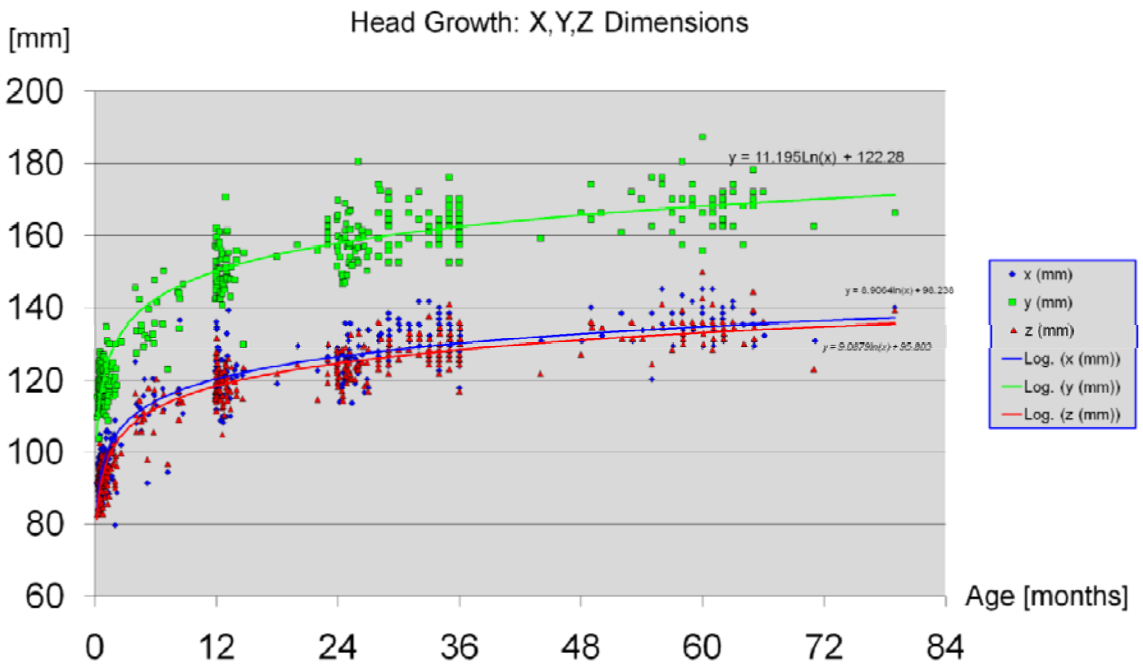
Minimize:

$$E(m,b) = \sum_{i=1}^{N} \left((mx_i + b) - y_i \right)^2$$



Regression: Modeling Head Size

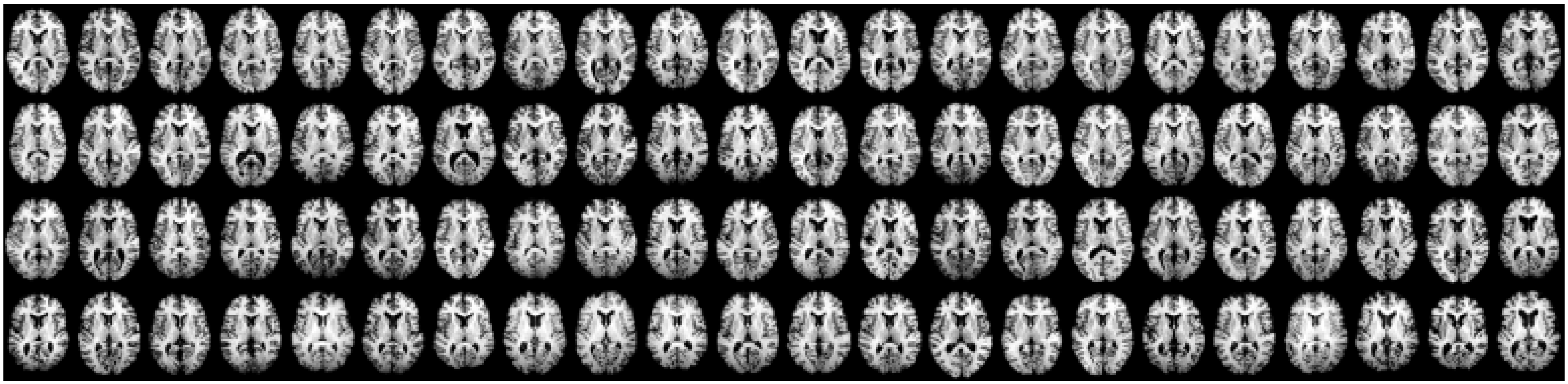




Longitudinal modeling of head size (N=411) based on MRI

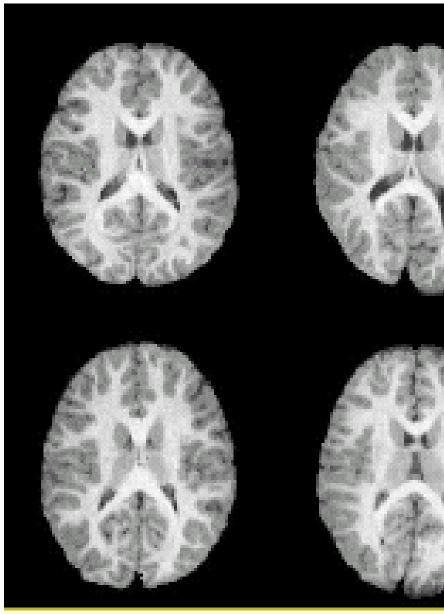
X,Y,Z: LR, AP, IS lengths

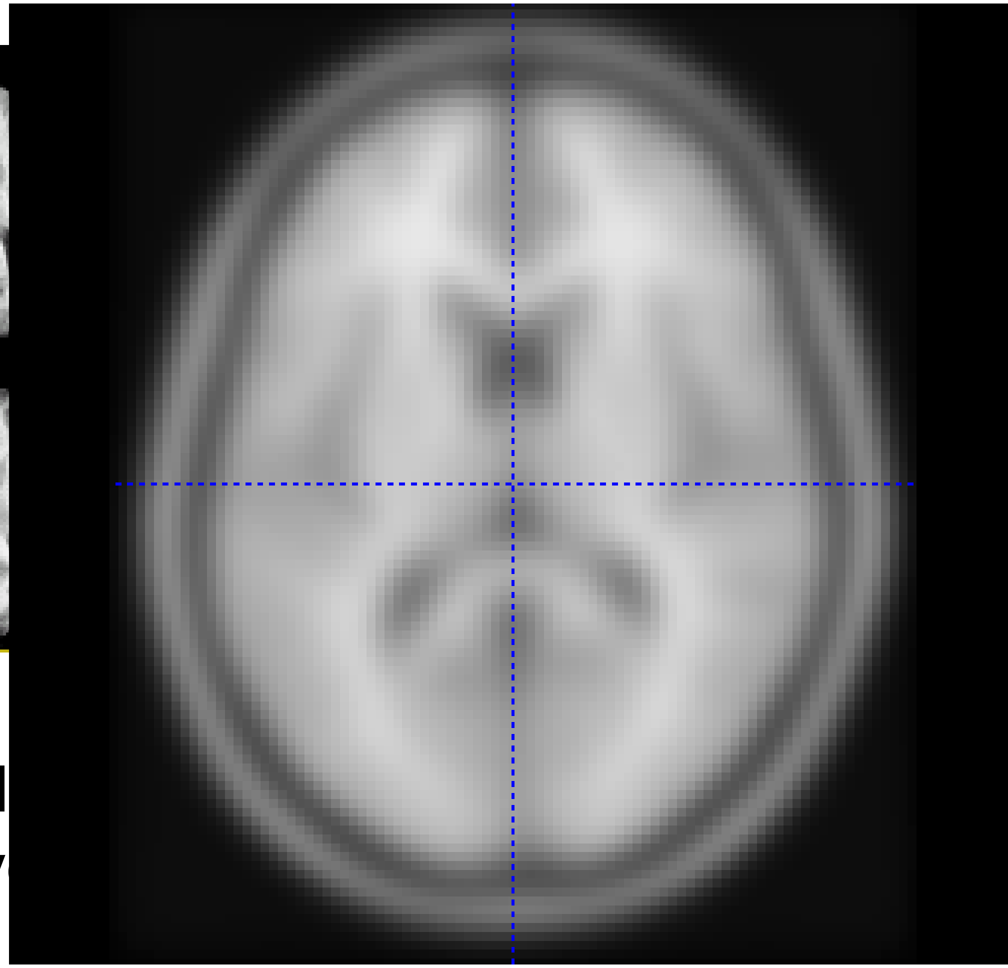
Example: Understanding the Aging Brain

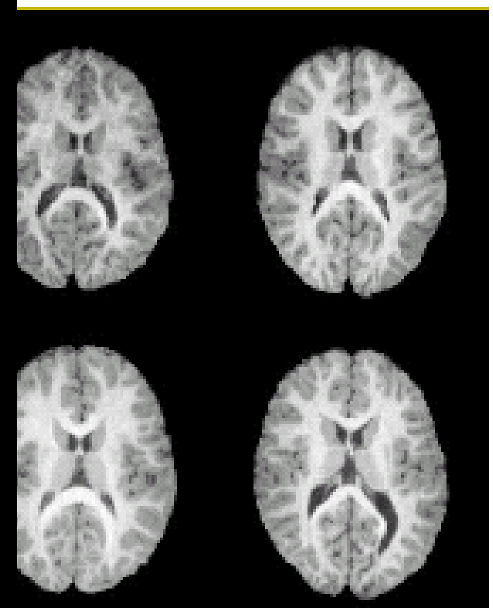


- 88 brain images, ages 20-80 yrs old
- Can we see a trend in how the brain changes as people get older?

Statistics on Images?







Given a col … s the Image
of the “Av … ariability”?

Linear Average does not
look like real image

Building of Population Averages: "Atlases"

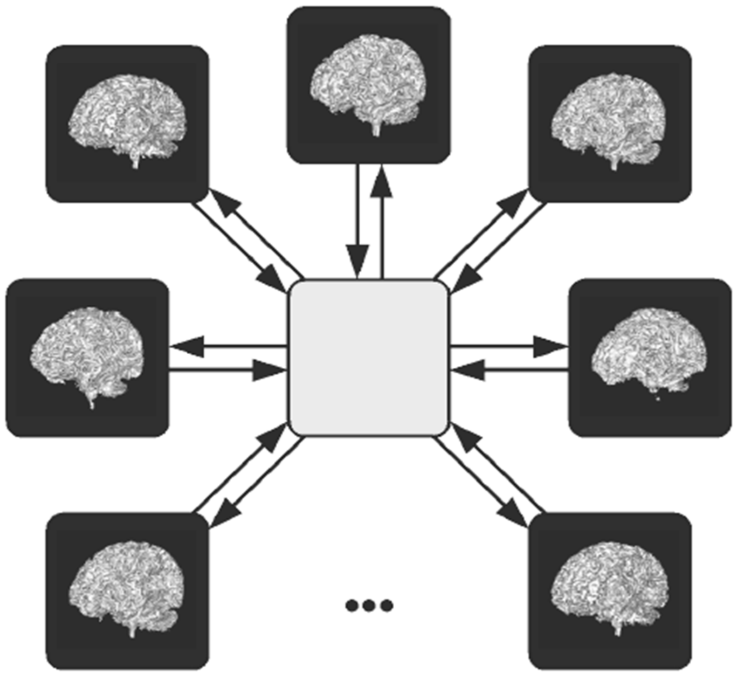


Figure 1. Template Construction Framework

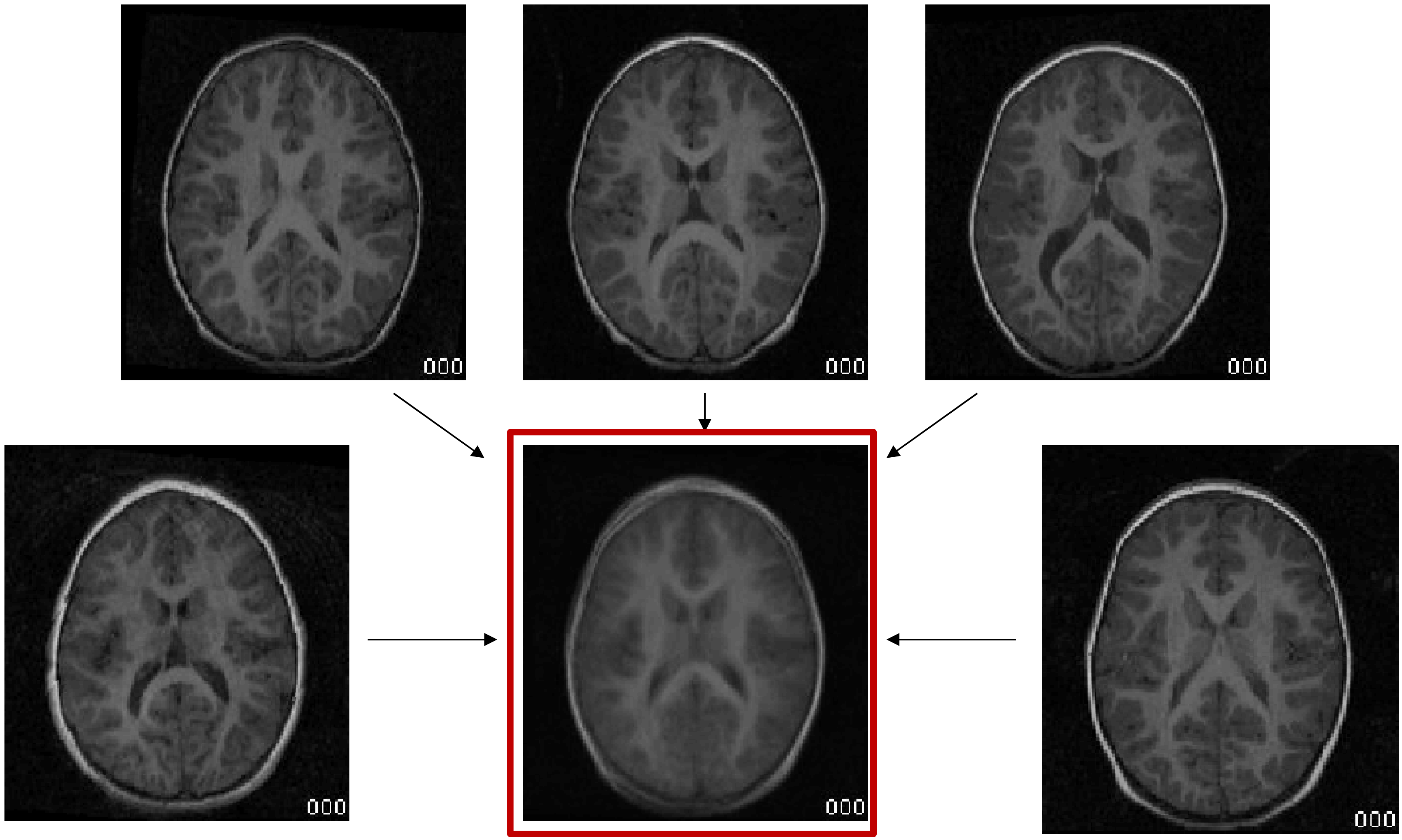
Motivation:

- Map population into common coordinate space
- Learn about normal variability
- Describe difference from normal
- Use as normative atlas for segmentation

$$\{\hat{h}_i, \hat{I}\} = \underset{h_i \in S, I}{\operatorname{argmin}} \sum_{i=1}^{N} E(I_i \circ h_i, I)^2 + D(e, h_i)^2$$

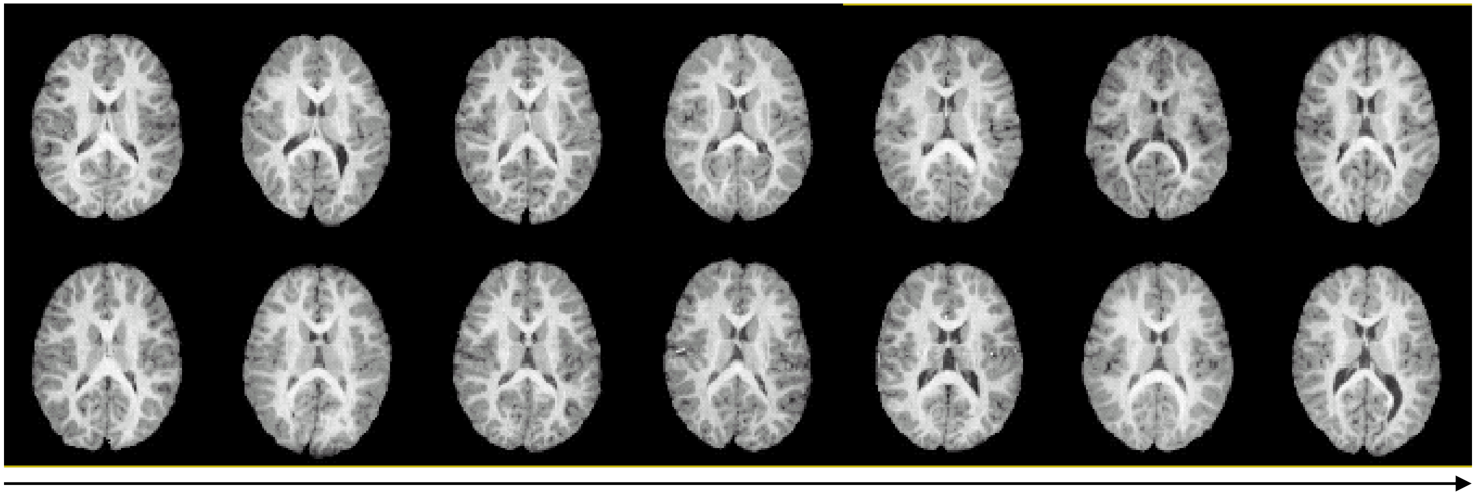
Joshi et al., Neuroimage 2004, Avants et al., Neuroimage 2004

Unbiased Atlas Building



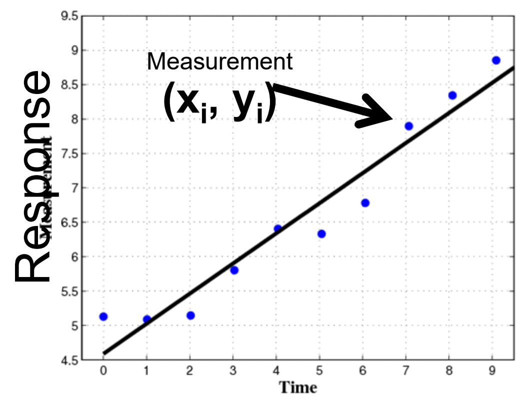
Joshi/Davis /Jomier/Gerig

Population Variability over Age



Age

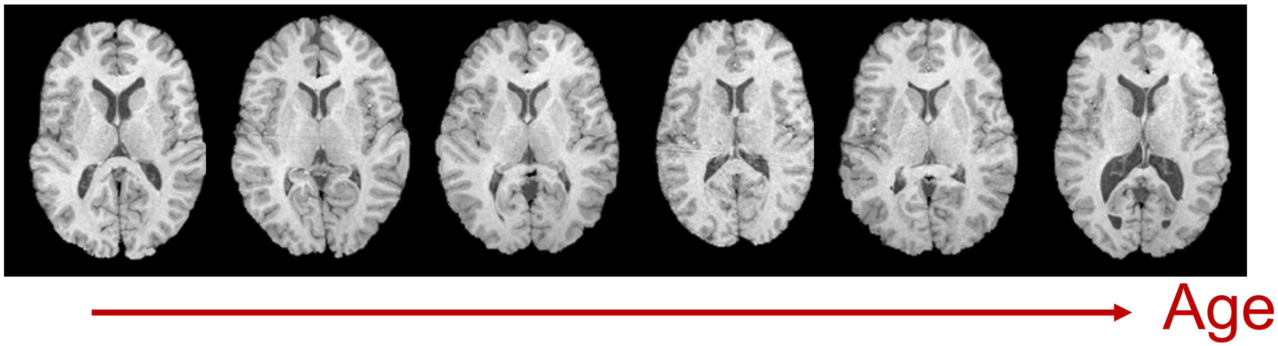
Normal Aging (50 subjects, 20 to 70 years)

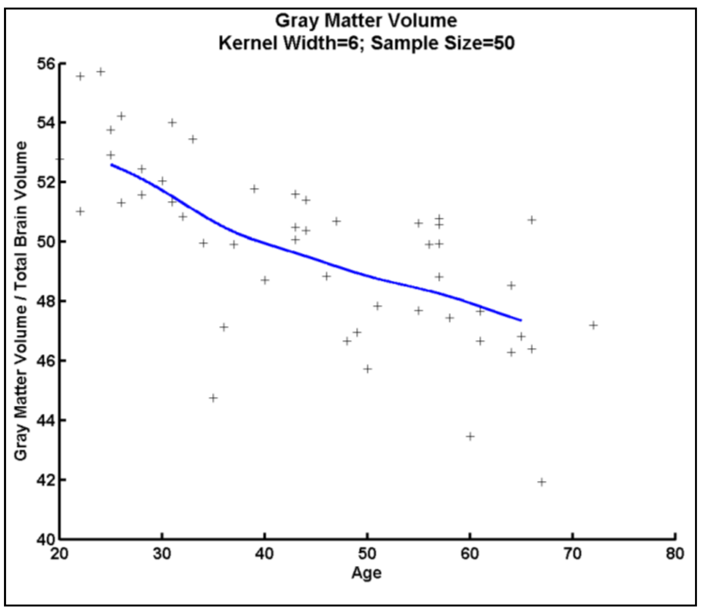


Predictor

Courtesy S. Joshi

Regression Model





Scalar Observations:

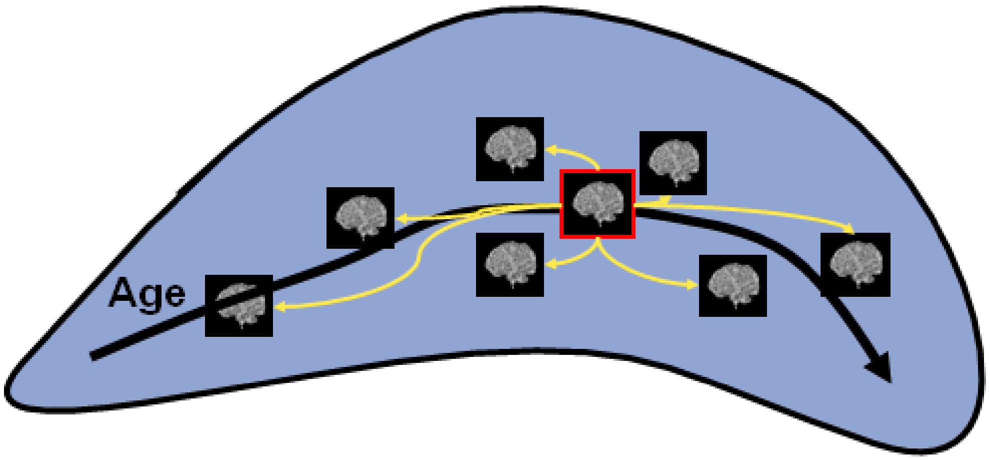
Volumes with associated age

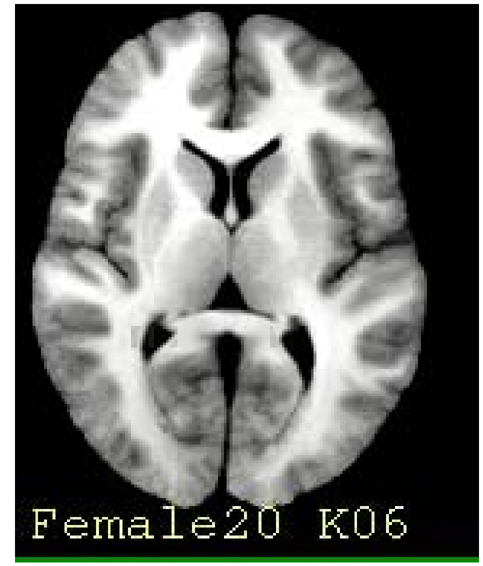
- Predictor: Age
- Response: Volume

Images as Observations:

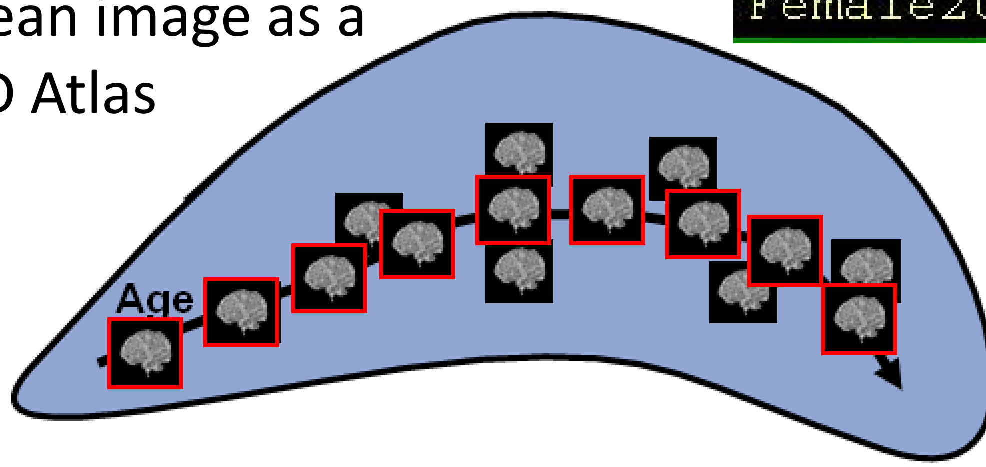
- Kernel regression with image "averaging" via group-wise registr.

3D Image Regression → 4D Atlas





Weighted Fréchet mean image as a function of age → 4D Atlas



Davis, Fletcher, Joshi (ICCV'07 Marr Prize, IJCV '10)

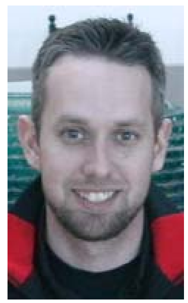
Contents

Quantification of Object Dynamics by Spatiotemporal Shape Analysis

James Fishbaugh

Guido Gerig

Marcel Prastawa



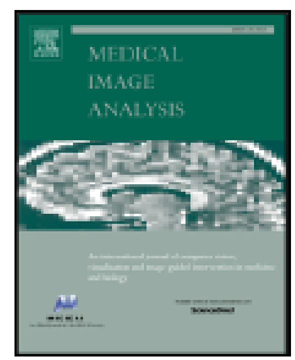
Stanley Durrleman, Xavier Pennec,
Nicholas Ayache, INRIA

Accepted Manuscript

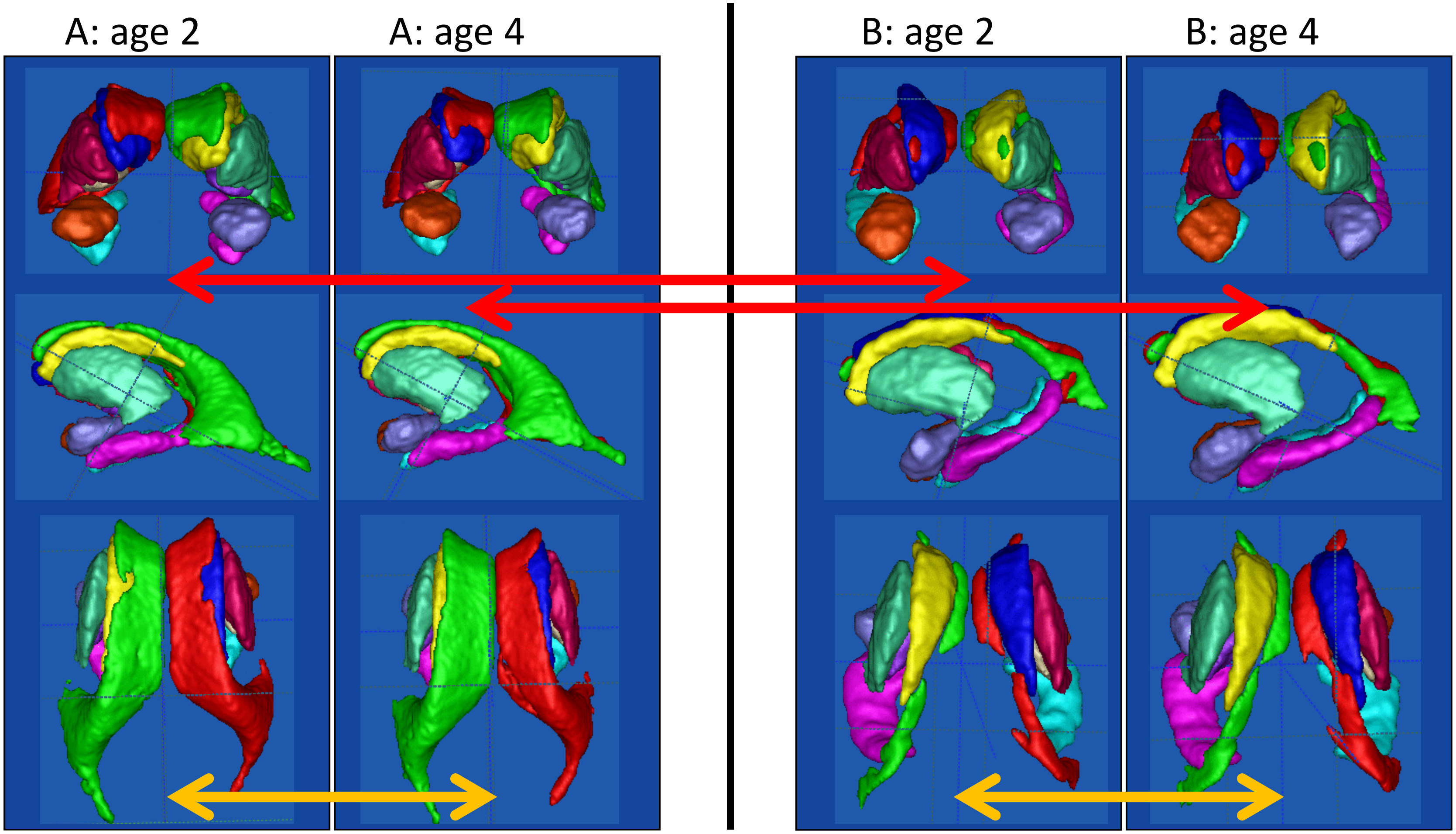
Longitudinal Modeling of Appearance and Shape and its Potential for Clinical Use

Guido Gerig, James Fishbaugh, Neda Sadeghi

PII: S1361-8415(16)30092-5
DOI: 10.1016/j.media.2016.06.014
Reference: MEDIMA 1133



Example Infant Study: Cross-sectional vs. Longitudinal



Cross-sectional: Huge changes between sets of shapes

Longitudinal: Subtle changes of sets of shapes with time

Shape and Registration

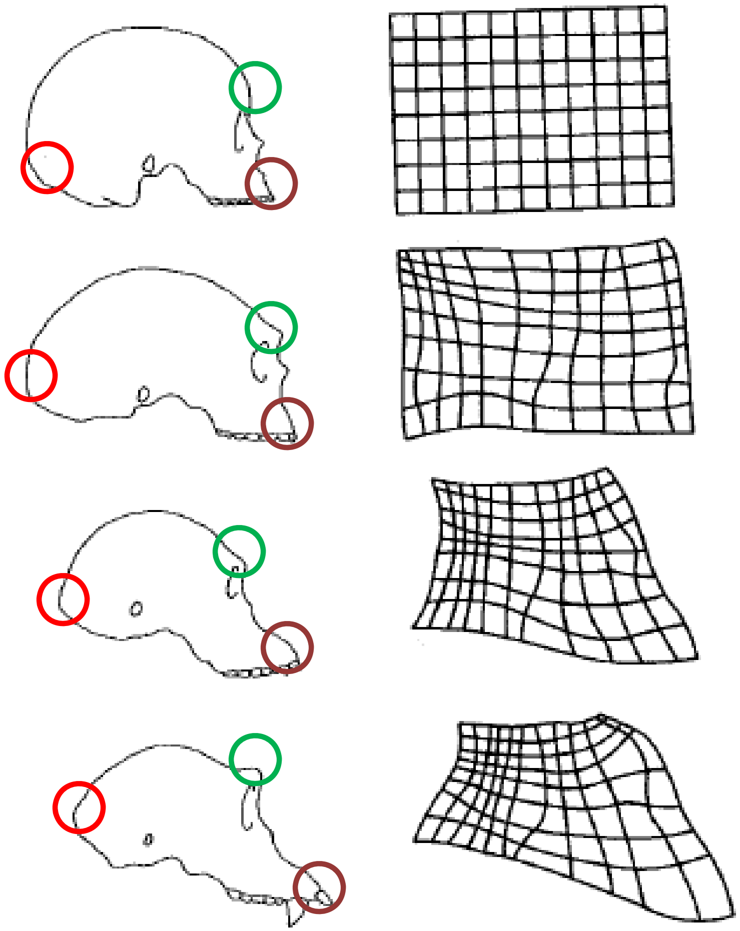


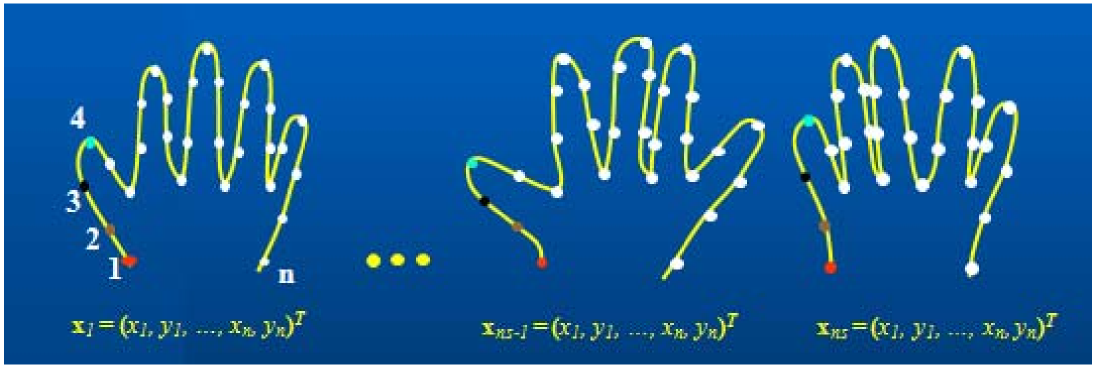
FIGURE 1.7. *Side view of skulls. From top to bottom: modern human, Neanderthal, australopithecine, chimpanzee. To the right of each skull is a coordinate grid determined with Thompson's method of coordinates, with the modern human skull as the base image. Reproduced from Figure 3.53 of [131] by kind permission of Hong Kong University Press.*

Homology:

Corresponding (homologous) features in all skull images.

Ch. G. Small, The Statistical Theory of Shape

Geometric Correspondence: Shapes



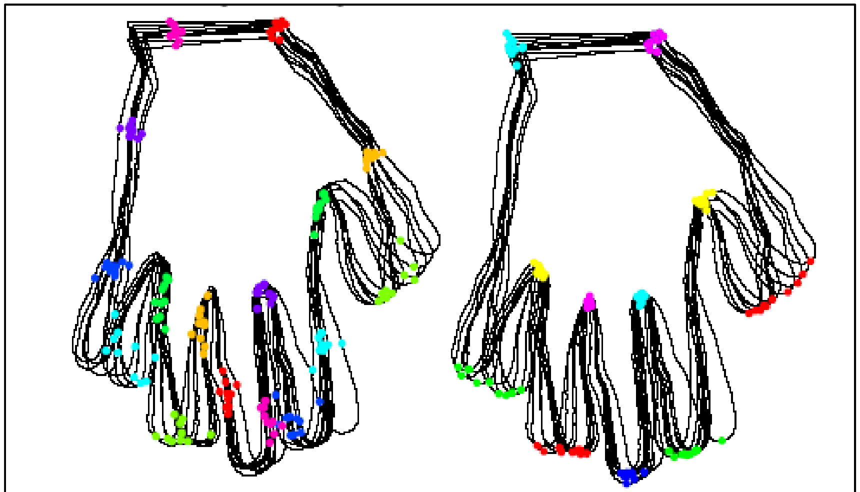
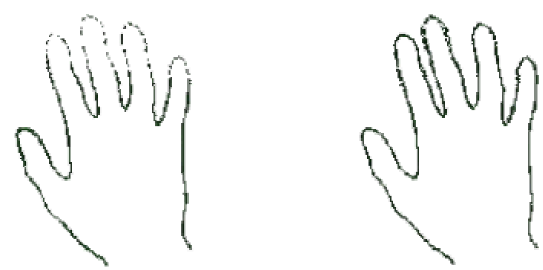


Figure 5.3. A subset of the correspondences and the alignment used to build the equally spaced Hand model.

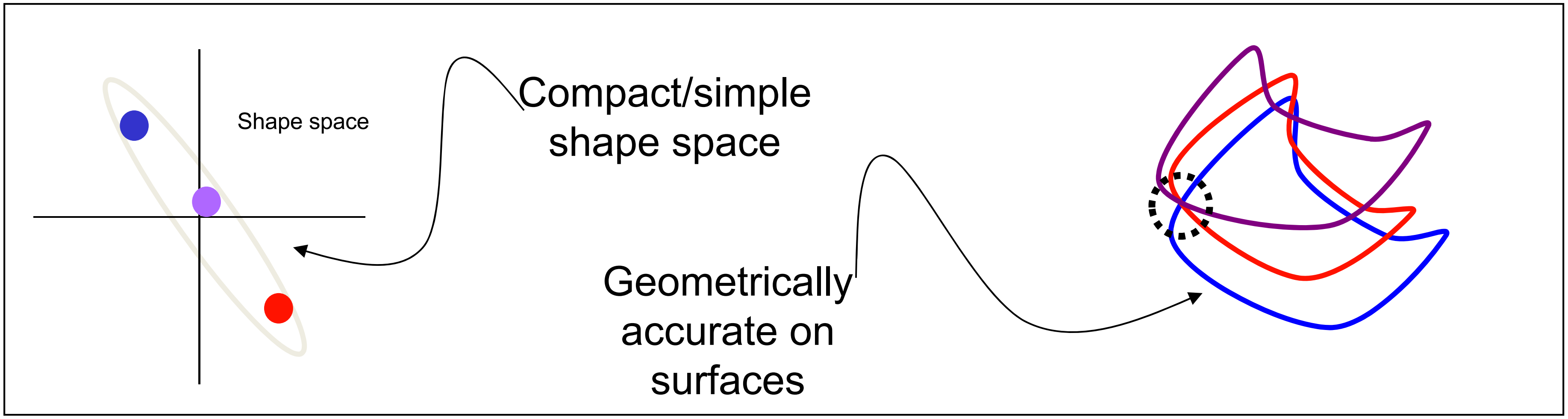
Figure 5.4. The manual landmarks and alignment used to build the manual Hand model.

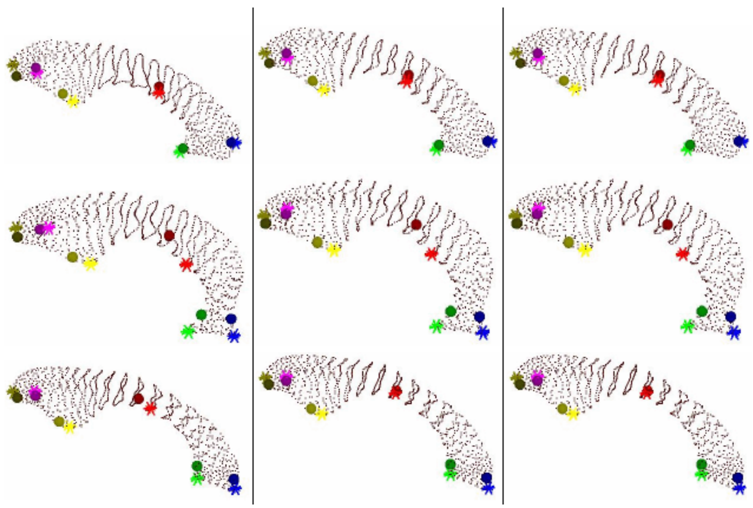
PDM Model (Cootes/Taylor):

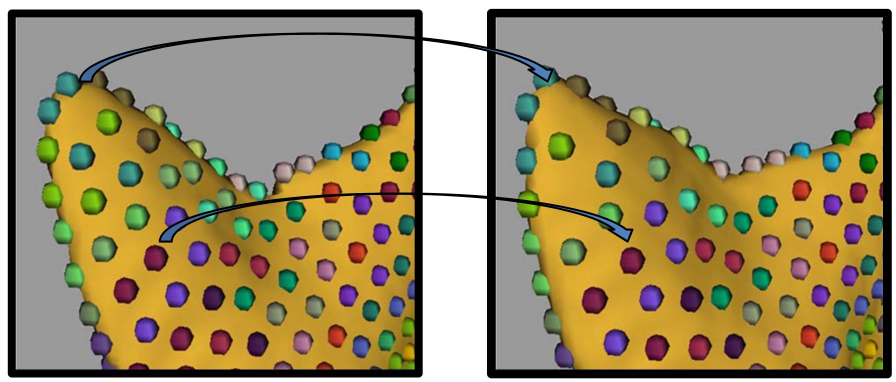
- Point to point correspondence for shape modeling
- PCA analysis
- Major eigenmodes of shape variability



Modeling a Shape Ensemble: Strategy for Landmark Placement



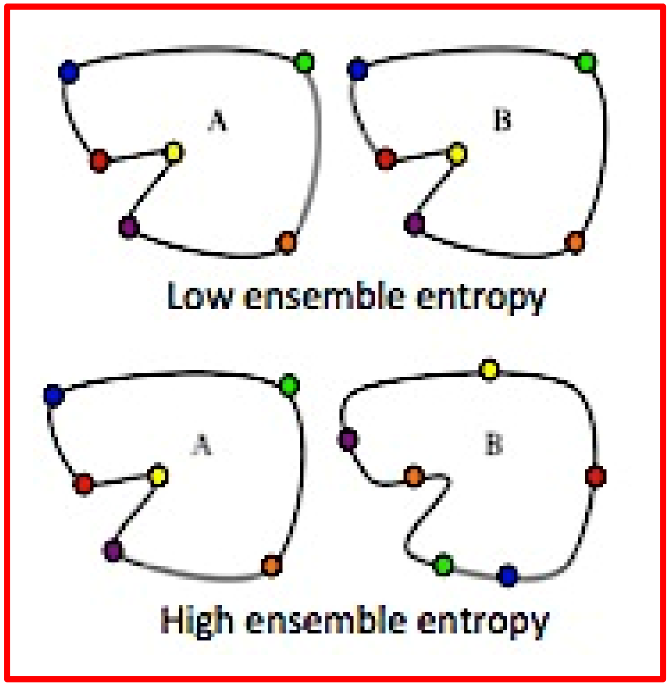




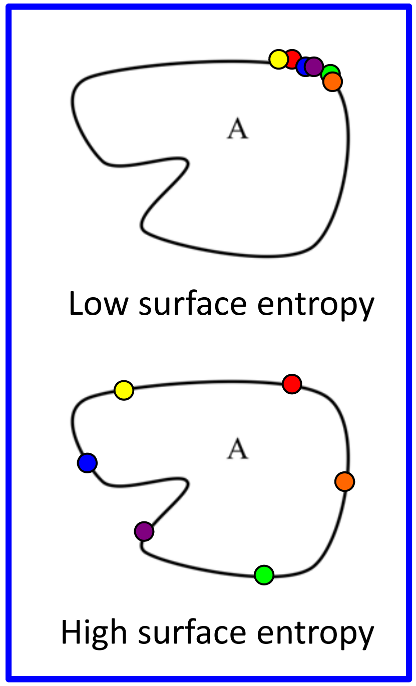
R. Whitaker, J. Cates, Uah

Entropy-based Particle Systems

- Surfaces are discrete point sets, no parameterization
- Dynamic particles, positions optimize the information of the system: ensemble entropy, surface entropy



low is better

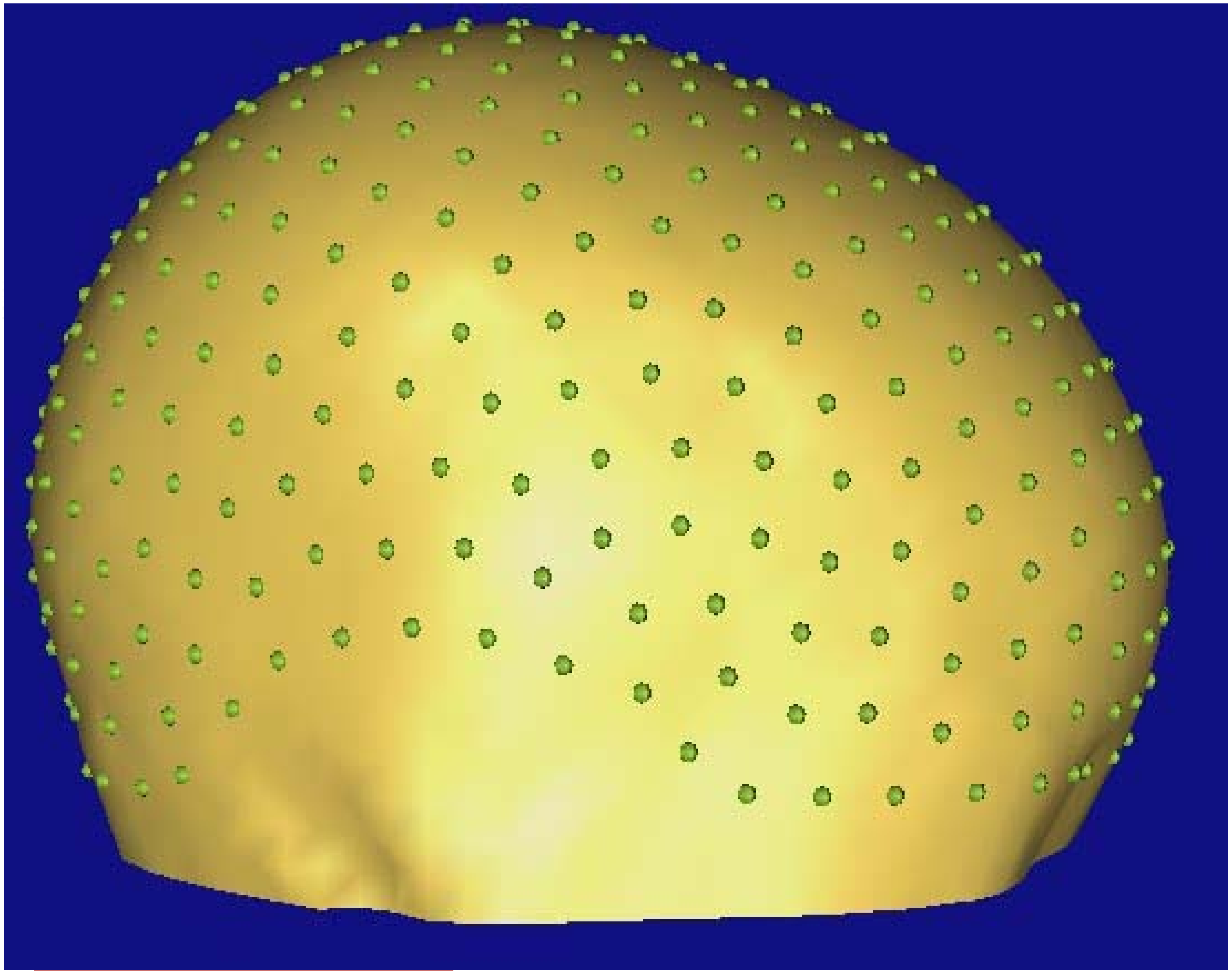


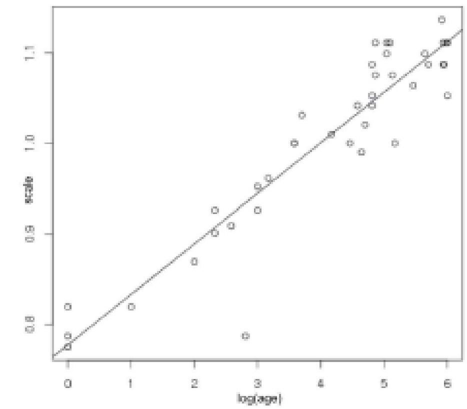
high is better

$$Q = H(Z) - \sum_k H(P^k)$$

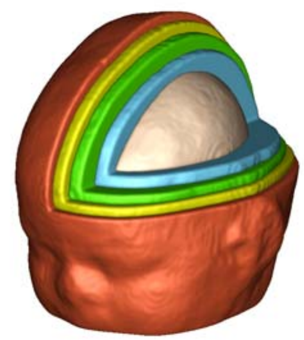
Oguz, Styner, Whitaker, Datar, Cates, 2009

Modeling Head Shape Change





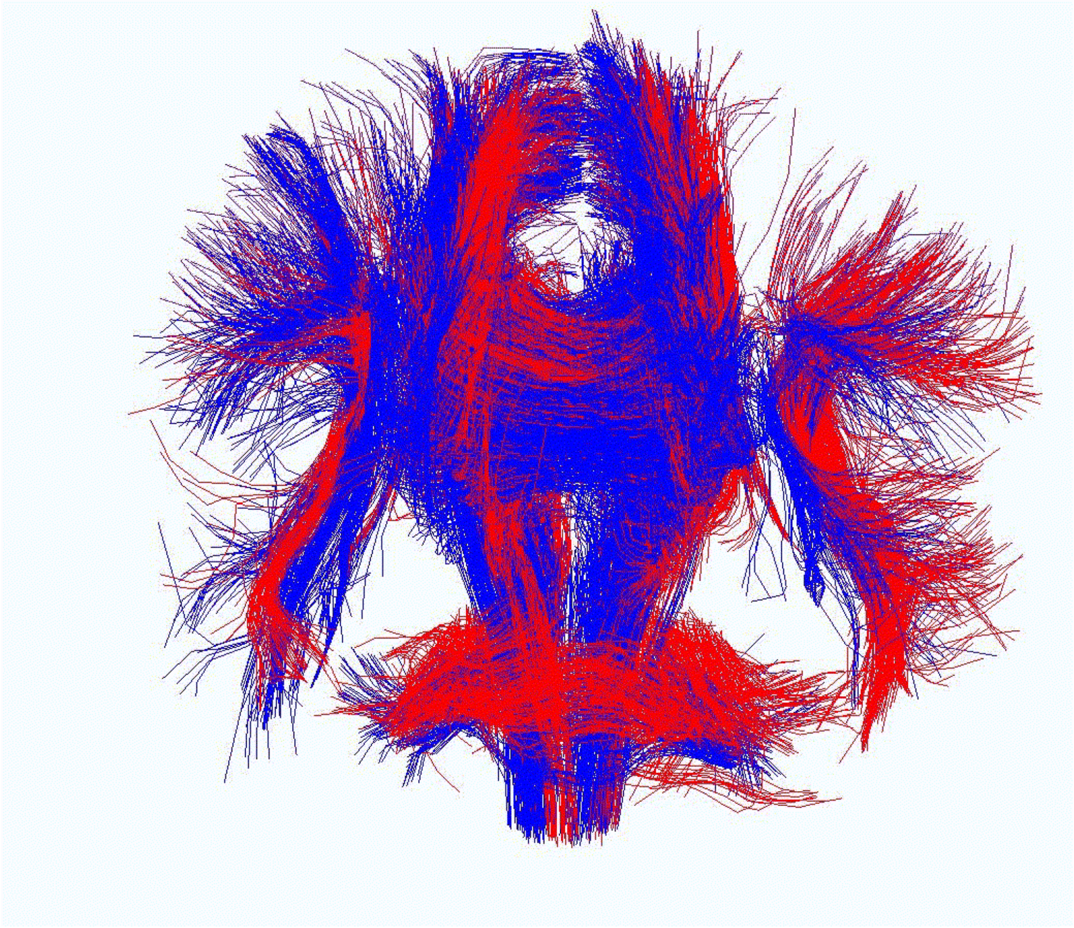
Changes in head size with age



Changes in head shape with age

Datar, Cates, Fletcher, Gouttard, Gerig, Whitaker, Particle-based Shape Regression, MICCAI 2009

Challenge: Registration without Point-to-Point Correspondences



Example:
Co-registration of whole-brain fiber tracts?

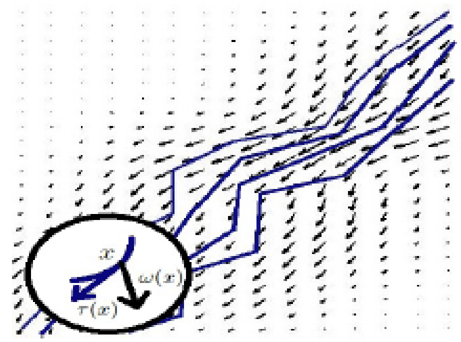
Durrleman, Pennec, Ayache et al.

“Correspondence-free” Registration: Currents

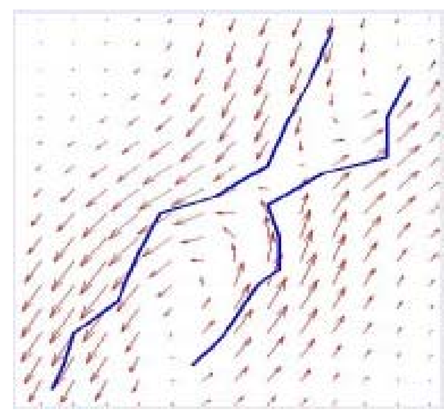
Topology and shape differences and noise can make point-to-point correspondence hard:

- **Currents**: Objects that integrate vector fields
- **Shape**: Oriented points = Set of normals (tangents)
- **Space of Currents**: Vector Space
- **Distance** between curves:

$$d(L_1, L_2)^2 = \int_{L_1} \omega_1(x)^t \tau_1(x)dx + \int_{L_2} \omega_2(x)^t \tau_2(x)dx - \int_{L_1} \omega_2(x)^t \tau_1(x)dx - \int_{L_2} \omega_1(x)^t \tau_2(x)dx$$



$$L(\omega) = \sum_{i=1\ldots4} \int_{L_i} \omega(x)^t \tau(x) d\lambda(x)$$

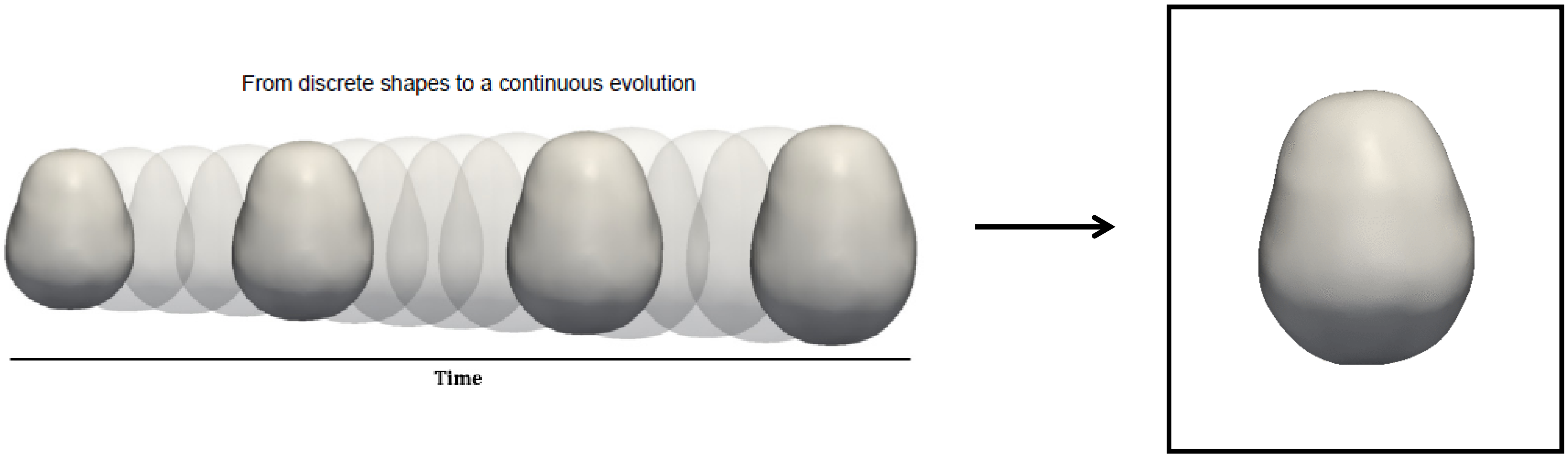


[Glaunes2004] Glaunes, J., Trouve, A., Younes, L. Diffeomorphic matching of distributions: a new approach, … CVPR 2004.

[Durrleman2008] S. Durrleman, X. Pennec, A. Trouvé, P. Thompson, N. Ayache, Inferring Brain Variability from Diffeomorphic Deformations of Currents: an integrative approach, Medical Image Analysis 2008

ACCELERATION-CONTROLLED SHAPE REGRESSION

4D Shape Modeling from Time-Discrete Data



- **Concept**: Given a set of time-discrete shapes, non-uniformly spaced, interpolate a continuous 4D growth model via shape regression.
- **Assumption**: Growth/degeneration of biological tissue is inherently smooth in space and time & nonlinear, locally varying process.
- **Method**: Continuous flow of diffeomorphisms via correspondence-free "currents". *Cost function = Data Matching + Regularity.*

Durrleman, Pennec, Ayache, Trouve, Gerig, MICCAI '09
Fishbaugh, Durrleman, Gerig, MICCAI '11, SPIE'12, MICCAI'12, IPMI'13

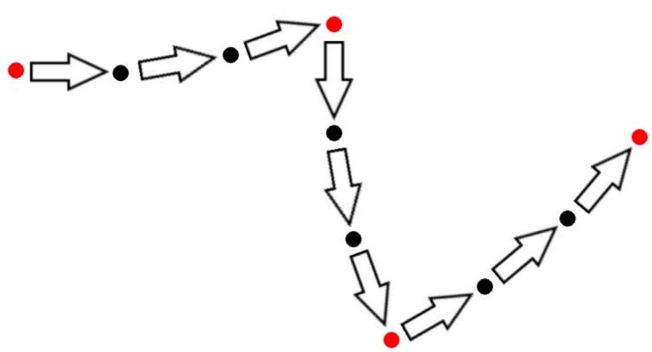
Key Observation

Piecewise geodesic regression [Durrleman et. al,. MICCAI 09]

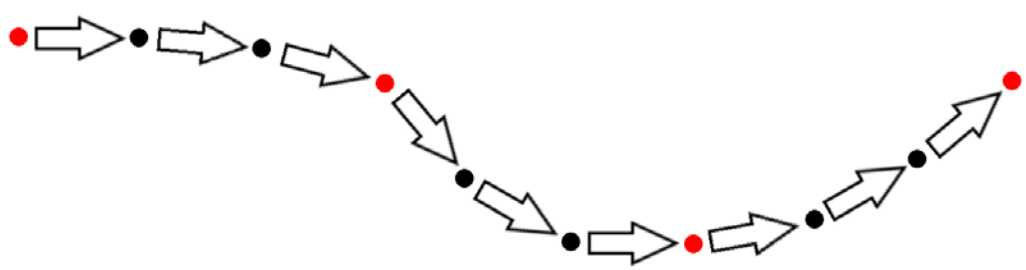
- Shape evolution modeled as the continuous flow of diffeomorphisms
- Geodesics interpolate between observations
- Extension of piecewise linear regression to space of diffeomorphisms

Cannot prevent a loss of regularity at target data

Due to discontinuities in the velocity field

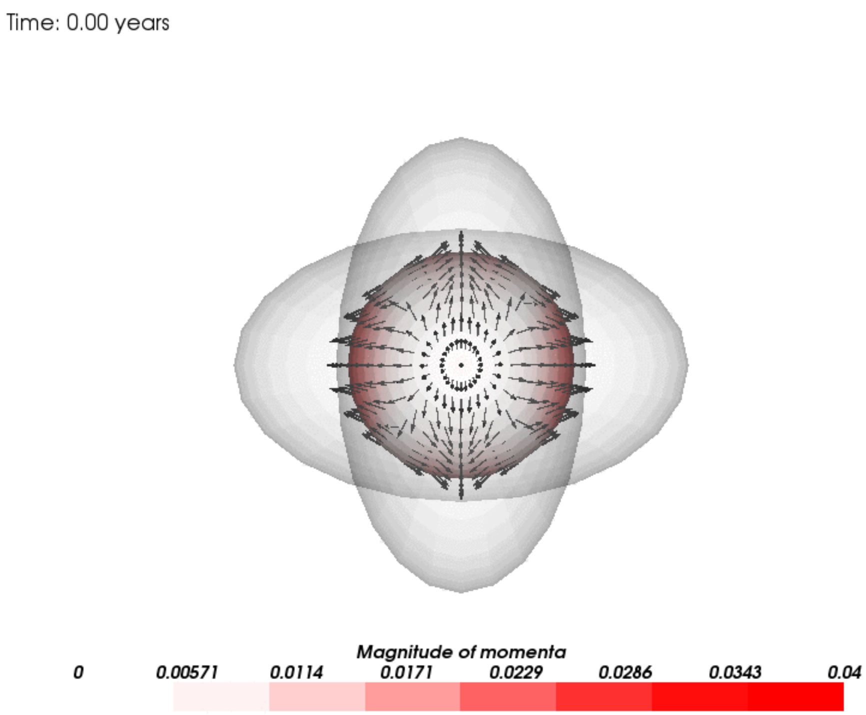


We might desire the velocity field to be differentiable everywhere

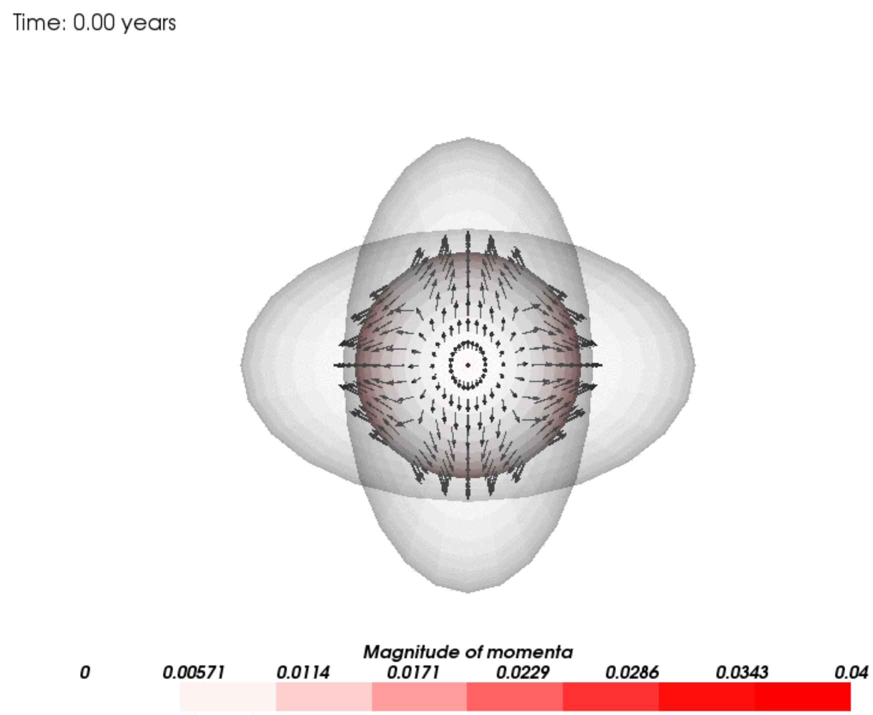


Piecewise Geodesic vs Acceleration Controlled

Synthetic experiment comparing piecewise geodesic and acceleration controlled shape regression



Piecewise geodesic



Acceleration controlled

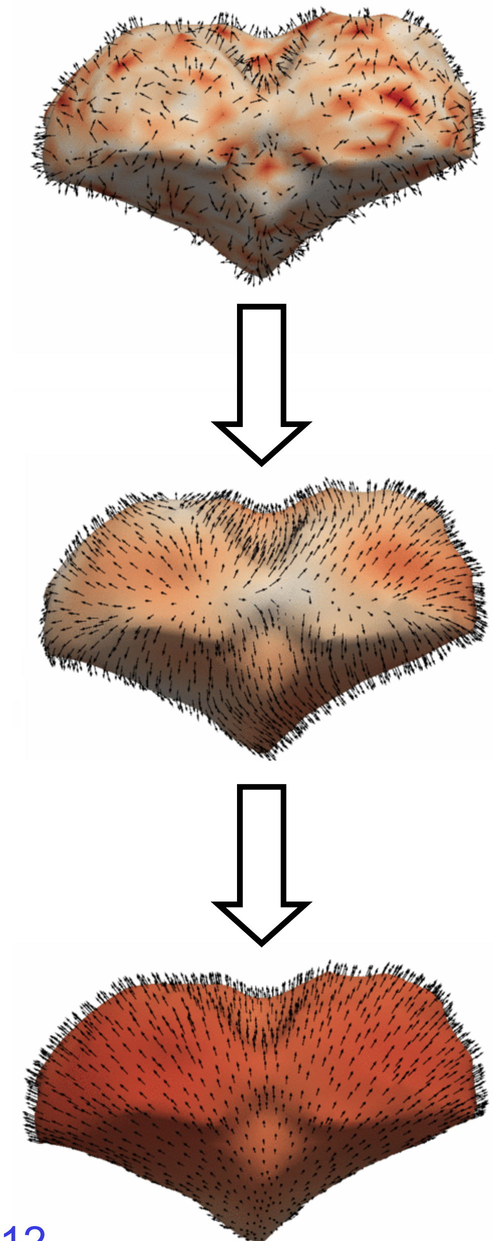
Acceleration Controlled Shape Regression

We define the acceleration field a(x(t)) as a vector field of the form

$$a(x(t)) = \sum_{i=1}^{N} K^V(x(t), x_i(t))\alpha_i(t)$$

x_i: the shape points carrying a point force vector α_i

$K^V(x, y) = exp(-\|x - y\|^2 / \lambda_V^2)$: a Gaussian kernel with standard deviation λ_V



Time varying deformation $\phi_t(x_i)$ given by:

$$\ddot{\phi}_t(x_i) = a(x_i(t))$$

$x_i(0)$: initial position

$\dot{x}_i(0)$: initial velocity

Fishbaugh, MICCAI 2011,12, 13, SPIE 2012

Regression Criterion

Let $\mathbf{x}(t)$, $\mathbf{a}(t)$, and $\boldsymbol{\alpha}(t)$ be the concatenation of the $x_i(t)$'s, $a_i(t)$'s, and the $\alpha_i(t)$'s.

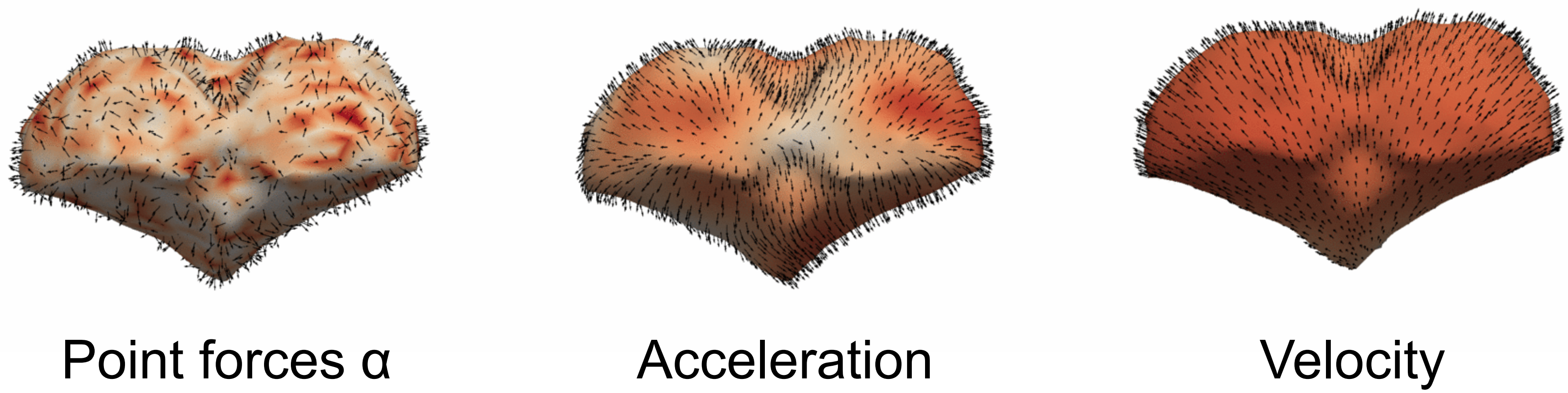
$$E(\dot{\mathbf{x}}(0), \boldsymbol{\alpha}(t)) = \sum_{t_i} \|\phi_{t_i}(\mathbf{x}(0)) - \mathbf{x}(t_i)\|_{W^*}^2 + \gamma \int_0^T \|\mathbf{a}(t)\|_V^2 \, dt$$

$\|\cdot\|_{W^*}$ is the norm on currents

$\|\mathbf{a}(t)\|_V^2 = \boldsymbol{\alpha}(t) K^V(\mathbf{x}(t), \mathbf{x}(t)) \boldsymbol{\alpha}(t)$

Acceleration Controlled Shape Regression

Evolution of cerebellum from 6 to 24 months



Interpolation Properties

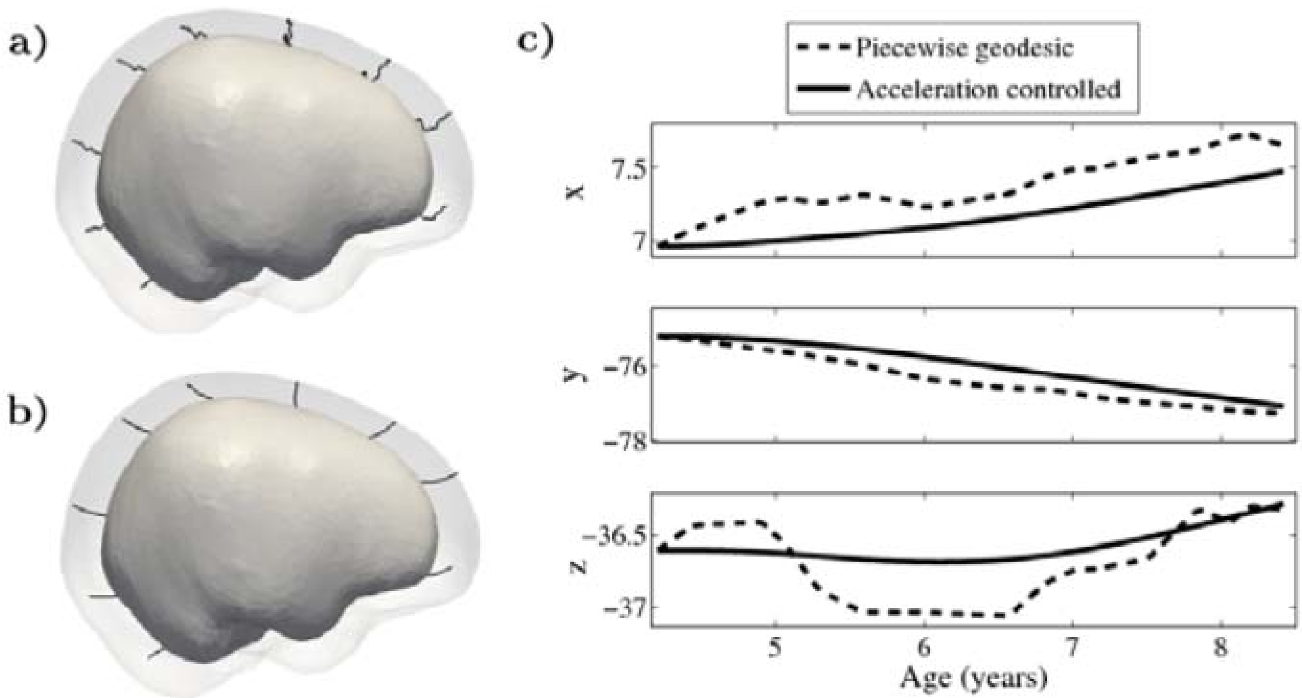
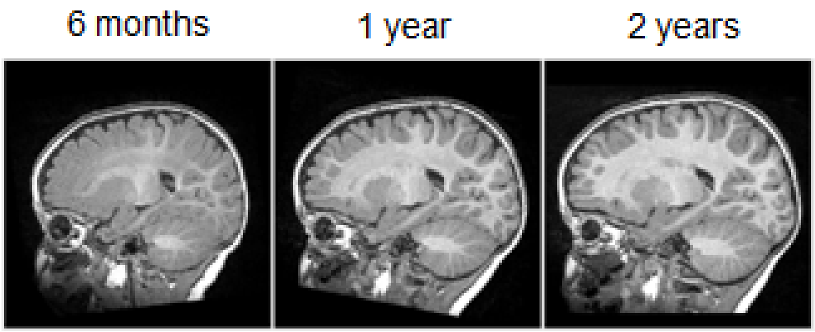
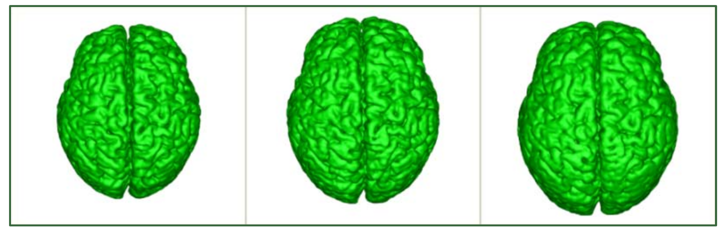


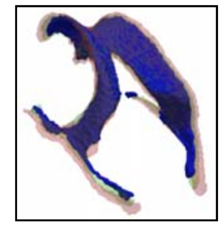
Fig. 1. a) and **b)** Shape evolution from baseline (solid) to final configuration (transparent) using a model based on piecewise geodesics (a) and our method (b) with point trajectories for selected particles displayed as black lines. **c)** The path of a point on the forebrain is decomposed into coordinates. Growth is estimated using 15 target shapes, highlighting the speed discontinuities present in the piecewise geodesic evolution.

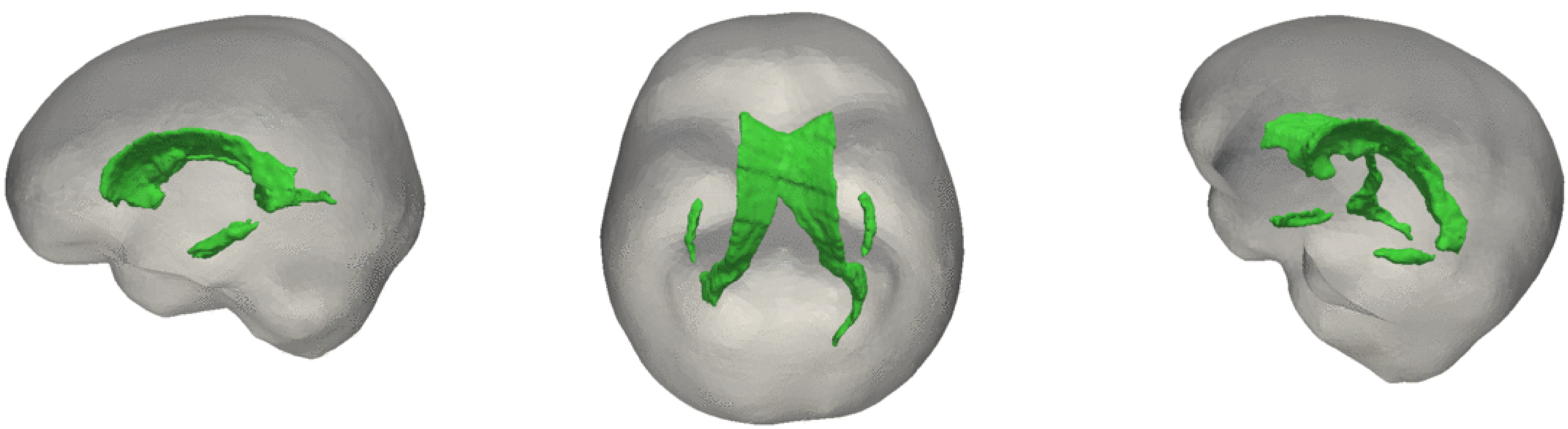
Fishbaugh et al., MICCAI 2011

Longitudinal Shape Regression



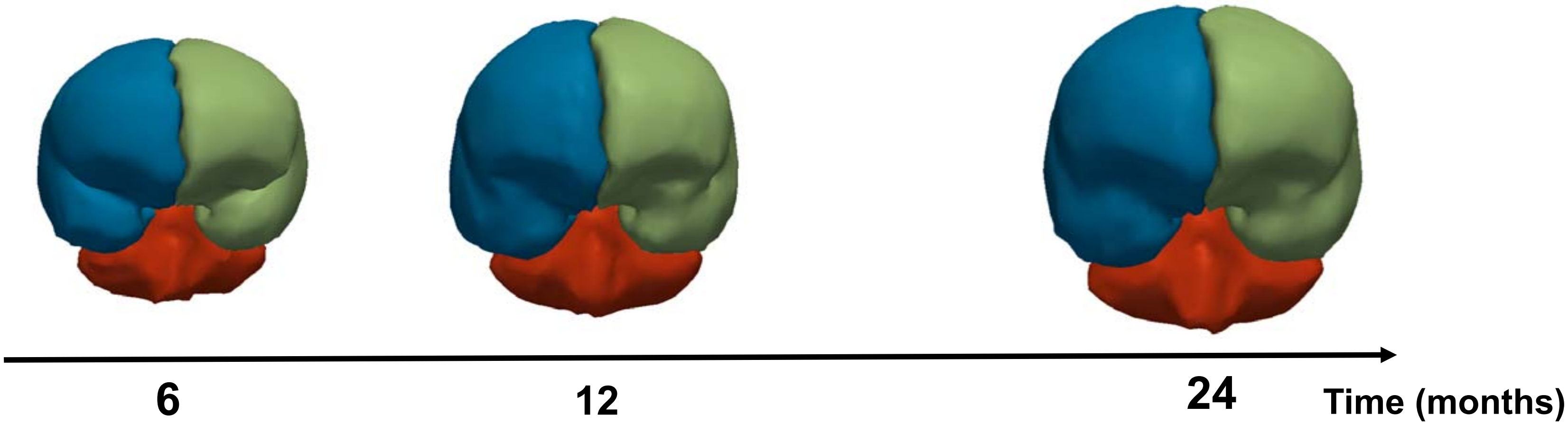




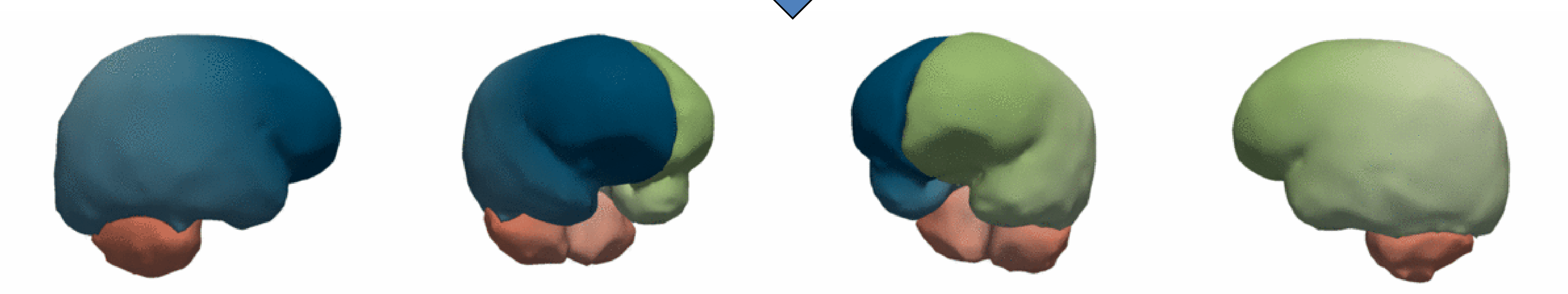


Durrleman, Fishbaugh, Gerig,
MICCAI 2011, MICCAI 2012

4D Shape Regression



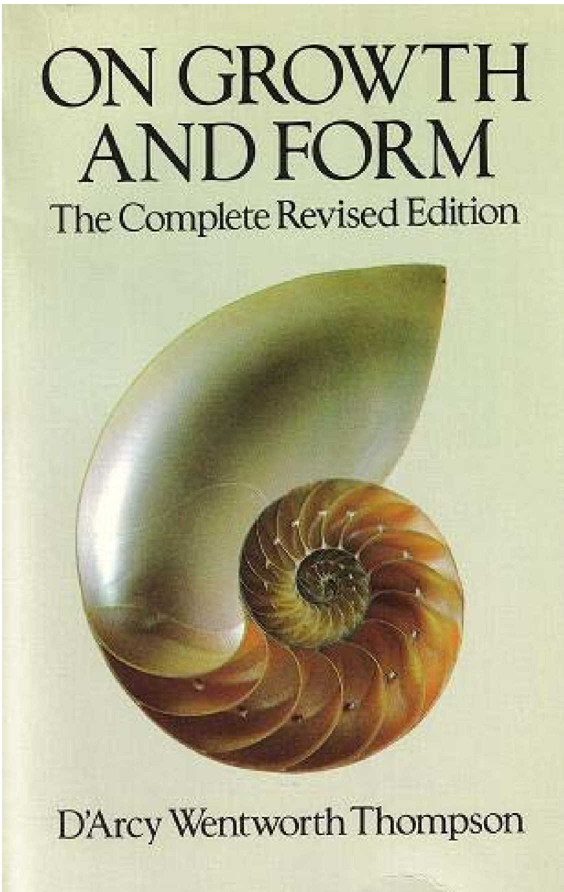
From discrete 3D shapes (6m,12m,24m) to continuous 4D shape model

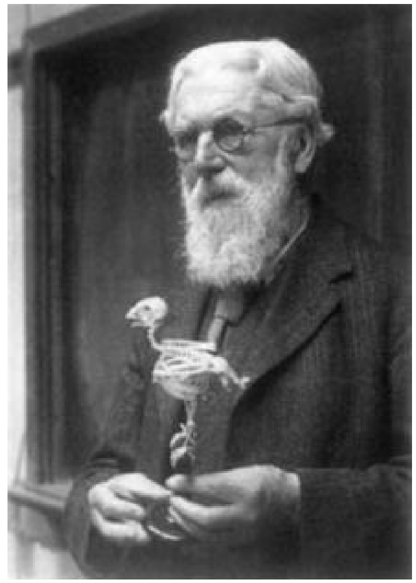


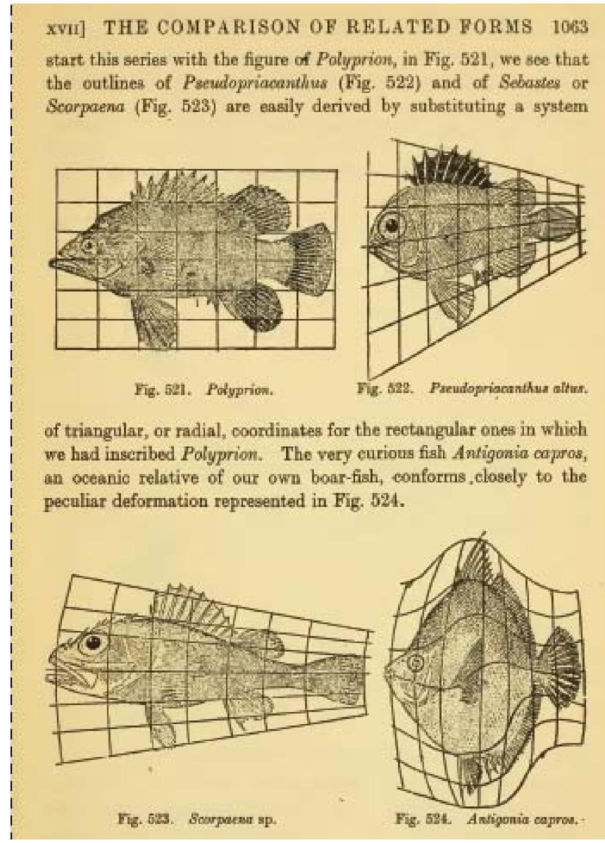
Fishbaugh, Durrleman, Gerig, MICCAI 2011, 2012

GEODESIC SHAPE/IMAGE REGRESSION

On Growth and Form







XVII] THE COMPARISON OF RELATED FORMS 1063

start this series with the figure of *Polyprion*, in Fig. 521, we see that the outlines of *Pseudopriacanthus* (Fig. 522) and of *Sebastes* or *Scorpaena* (Fig. 523) are easily derived by substituting a system

Fig. 521. *Polyprion*. Fig. 522. *Pseudopriacanthus altus*.

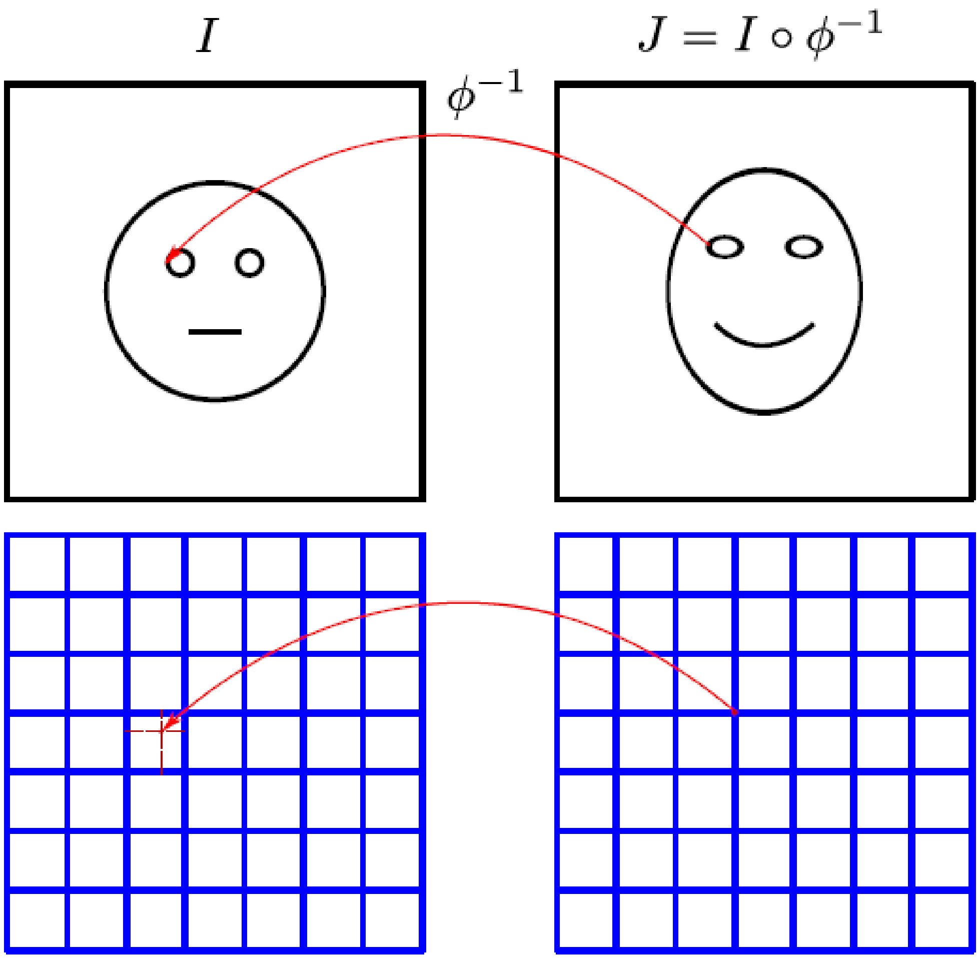
of triangular, or radial, coordinates for the rectangular ones in which we had inscribed *Polyprion*. The very curious fish *Antigonia capros*, an oceanic relative of our own boar-fish, conforms closely to the peculiar deformation represented in Fig. 524.

Fig. 523. *Scorpaena* sp. Fig. 524. *Antigonia capros*.

http://archive.org/download/ongrowthform00thom/ongrowthform00thom.pdf
http://ia700301.us.archive.org/10/items/ongrowthform00thom/ongrowthform00thom.pdf

D'Arcy Wentworth Thompson, On Growth and Form (1917, mathematics and biology)

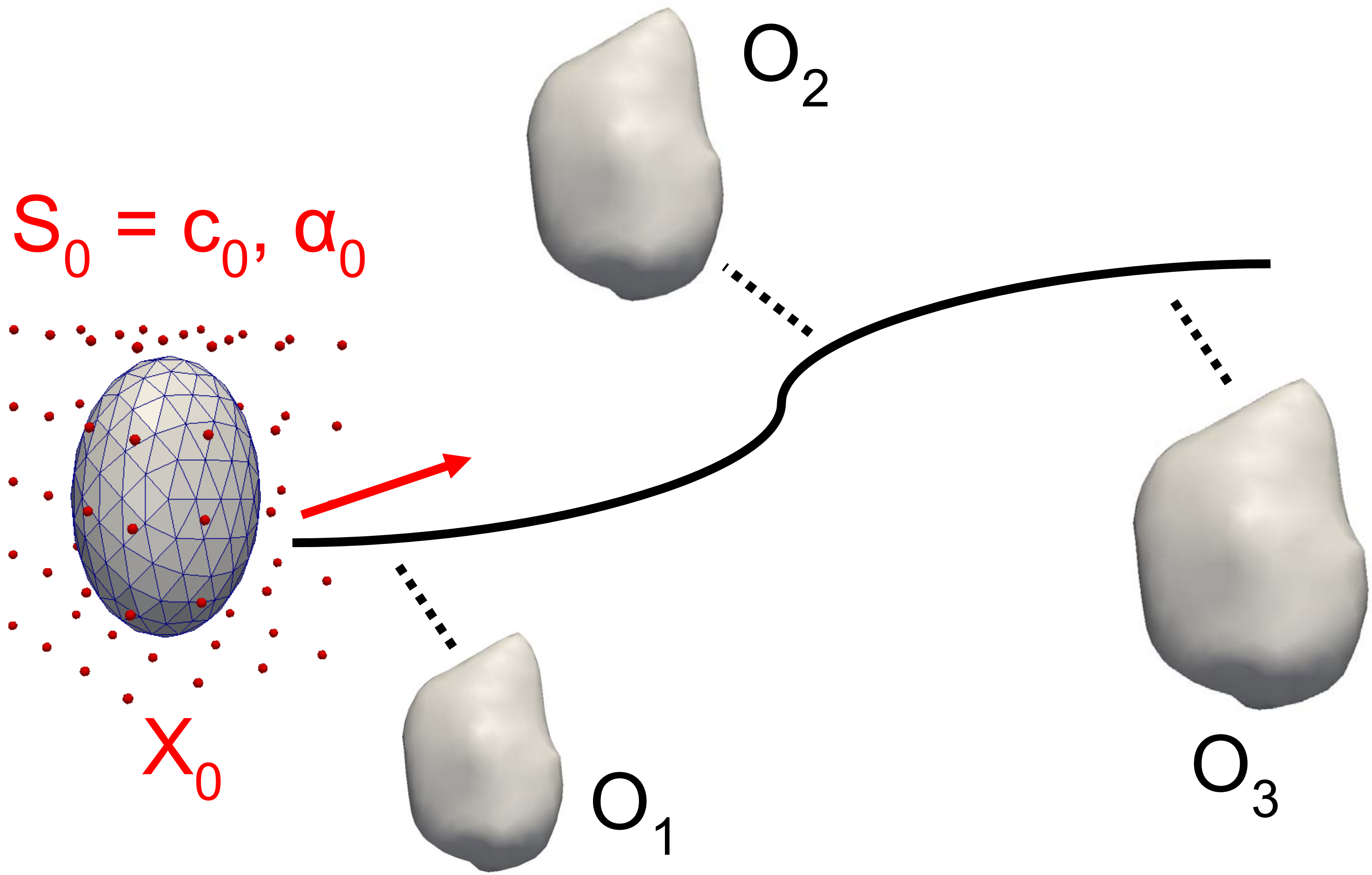
Ambient Space Deformation



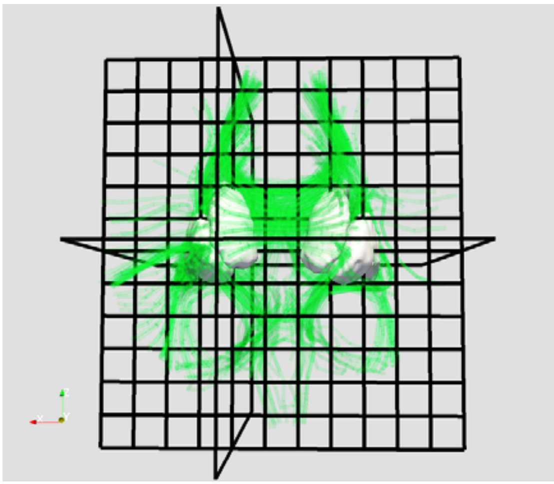
Change in geometric entities in images represented as transformations of the underlying coordinate grid.

Image: Nikhil Singh, PhD thesis Utah 2013

Geodesic Shape Regression

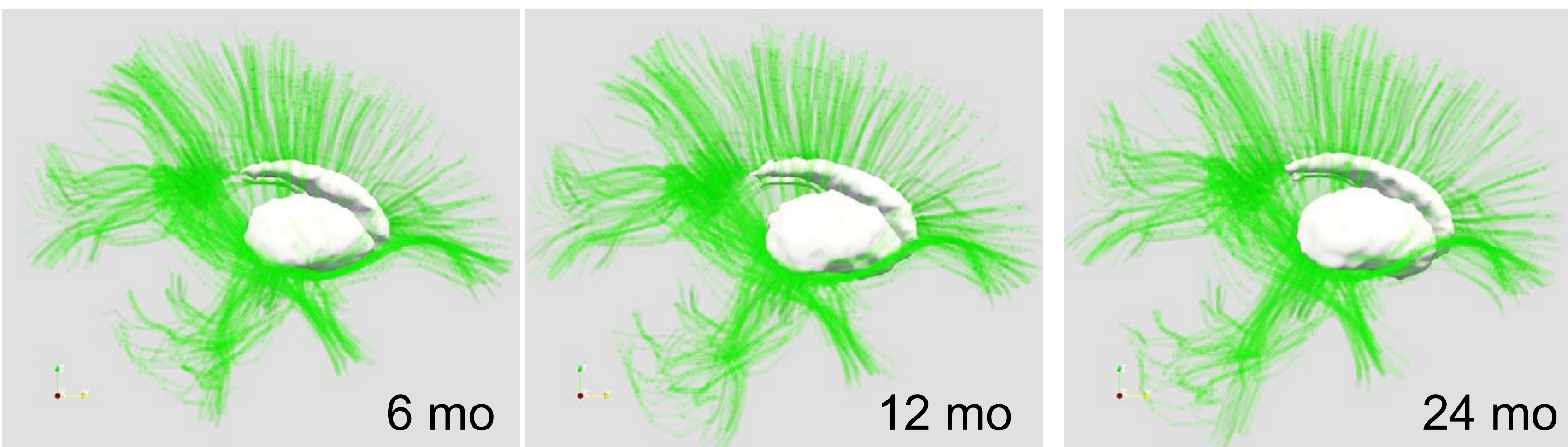


Pediatric Brain Development



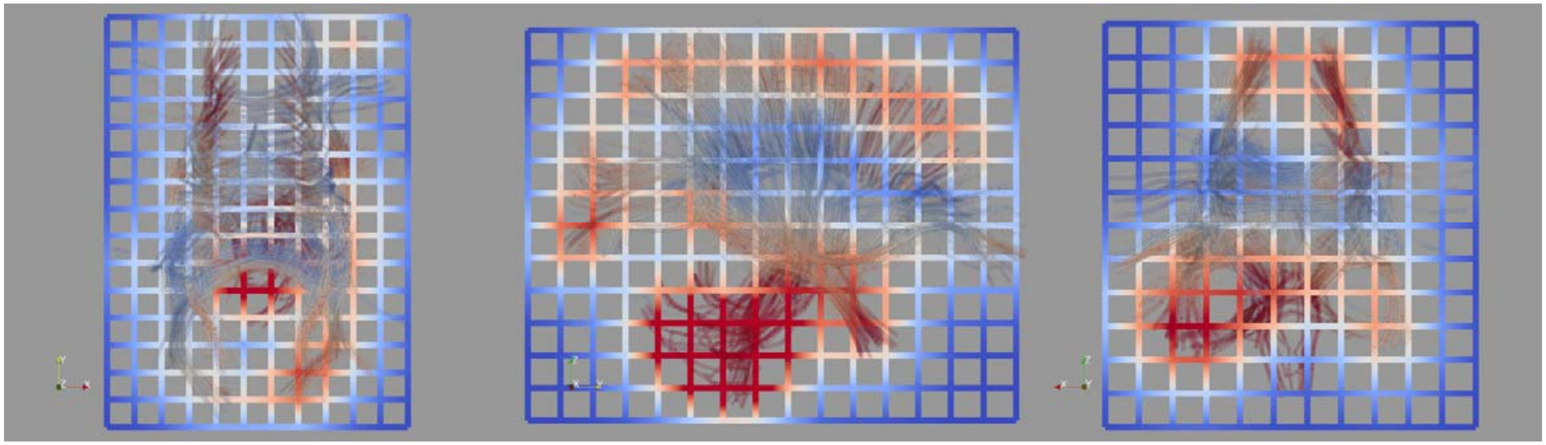
Multimodal shape regression:

- Combination of points, curves, meshes
- Here: fiber tracts from DTI and subcortical structures from T1w/T2w MRI

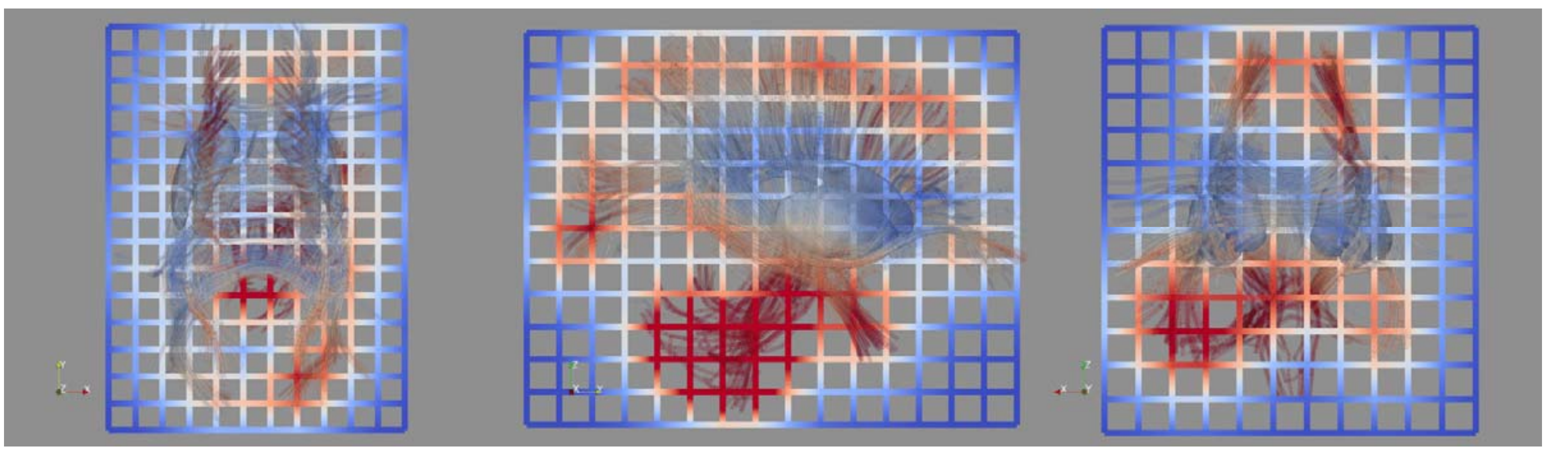


Pediatric Brain Development

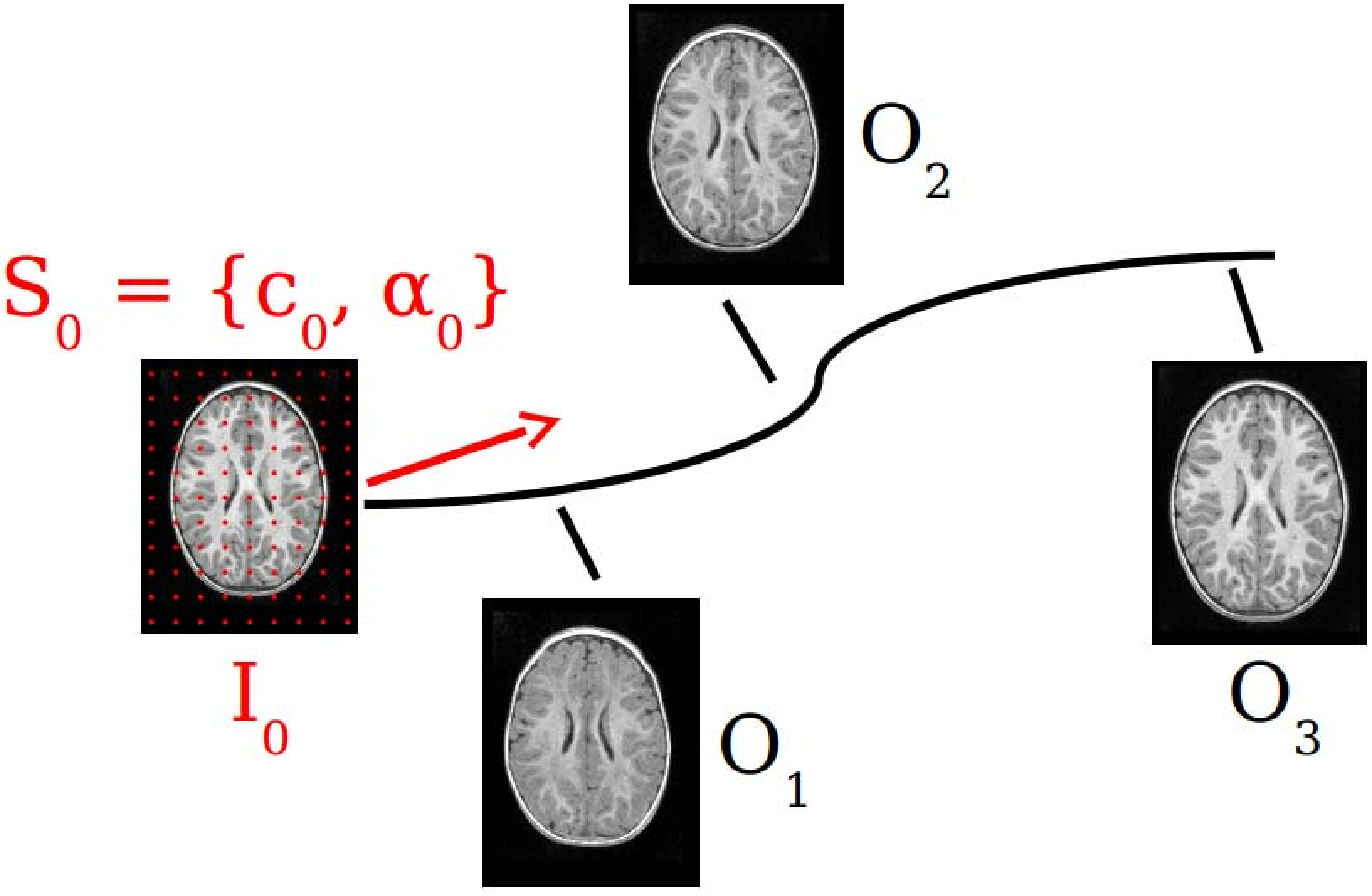
Regression with only fibers



Regression with fibers and anatomical shapes

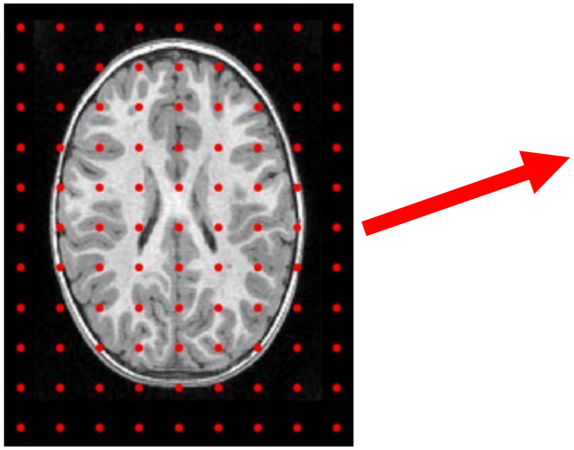


Geodesic Image Regression

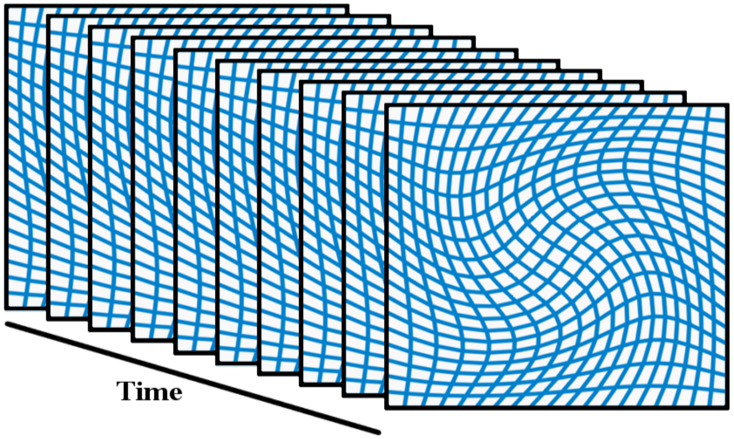


Summary of Method

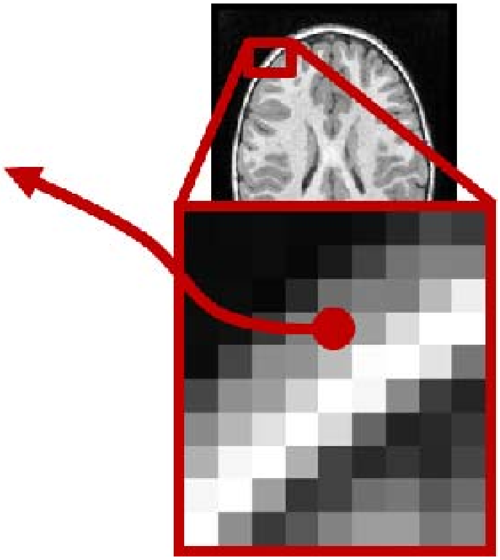
1) Shoot control points



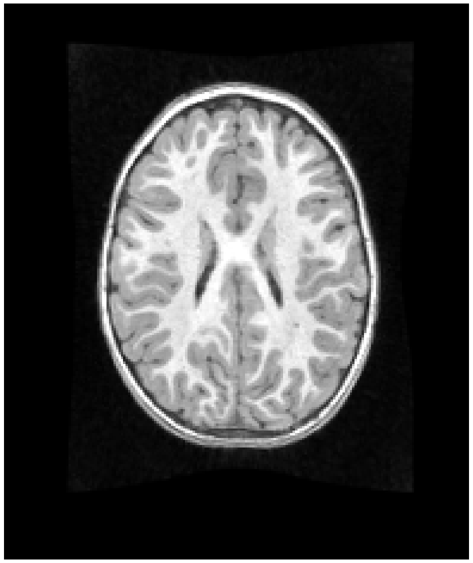
2) Trajectory defines flow



3) Flow pixel locations

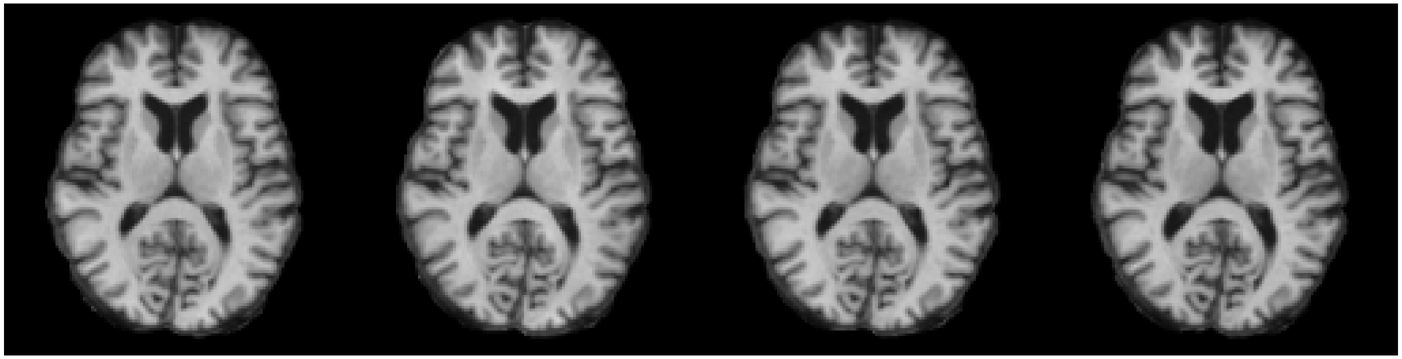


4) Interpolate in baseline image



Brain Atrophy in Alzheimer's Disease (3D)

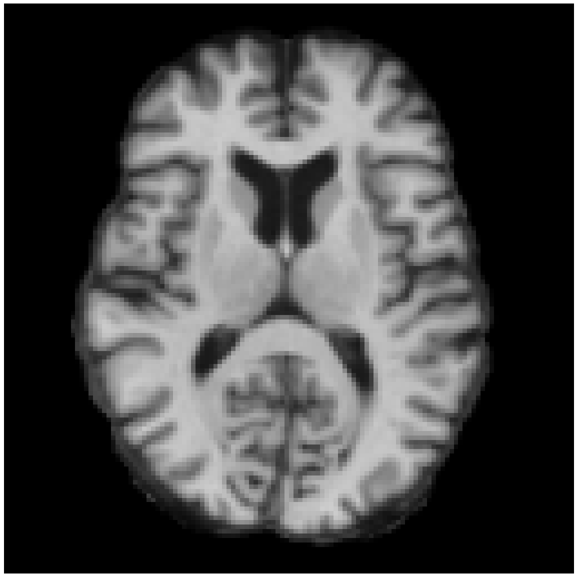
T1W images of **same** patient over time (~2,000,000 voxels)

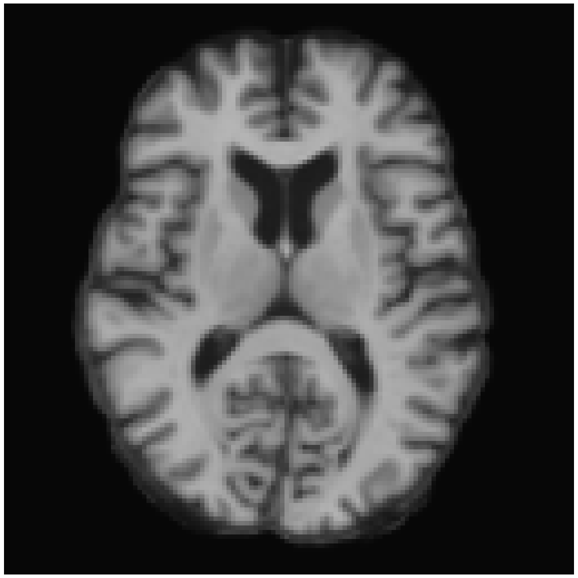


70.75 years **71.38 years** **71.78 years** **72.79 years**

Six years **predicted** brain atrophy

35,937





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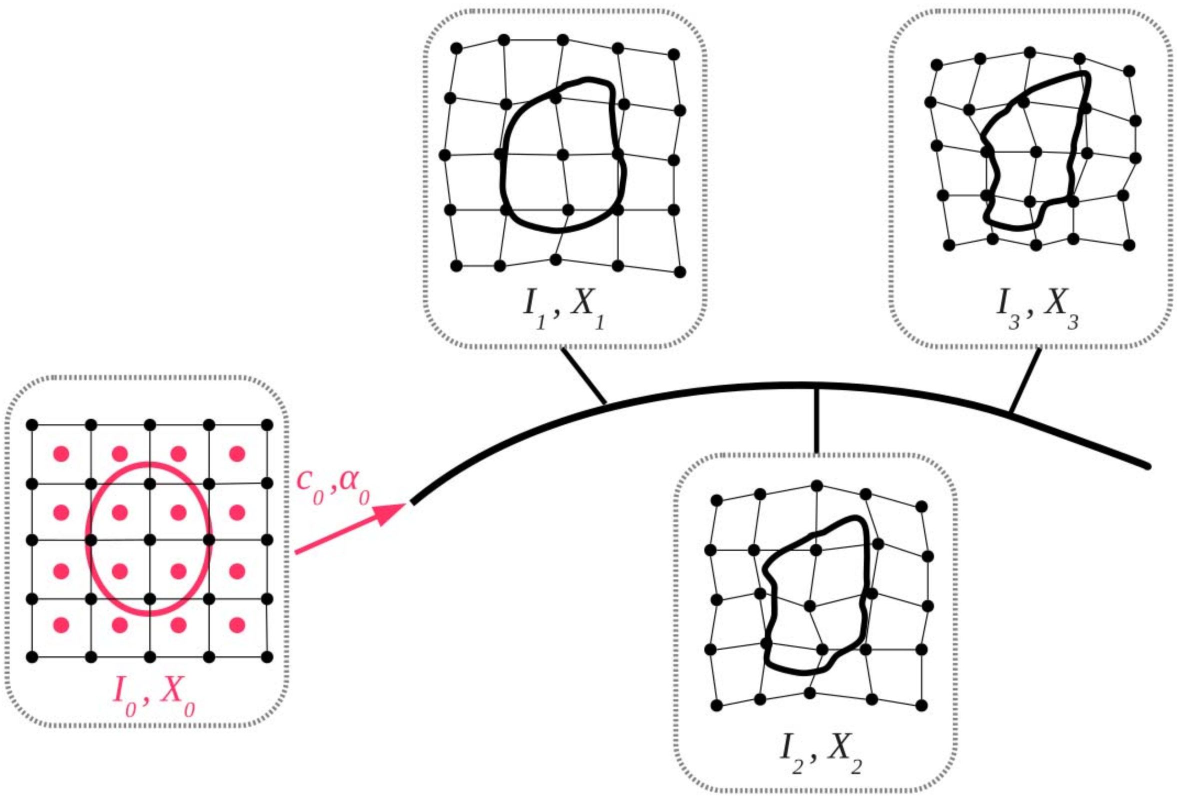
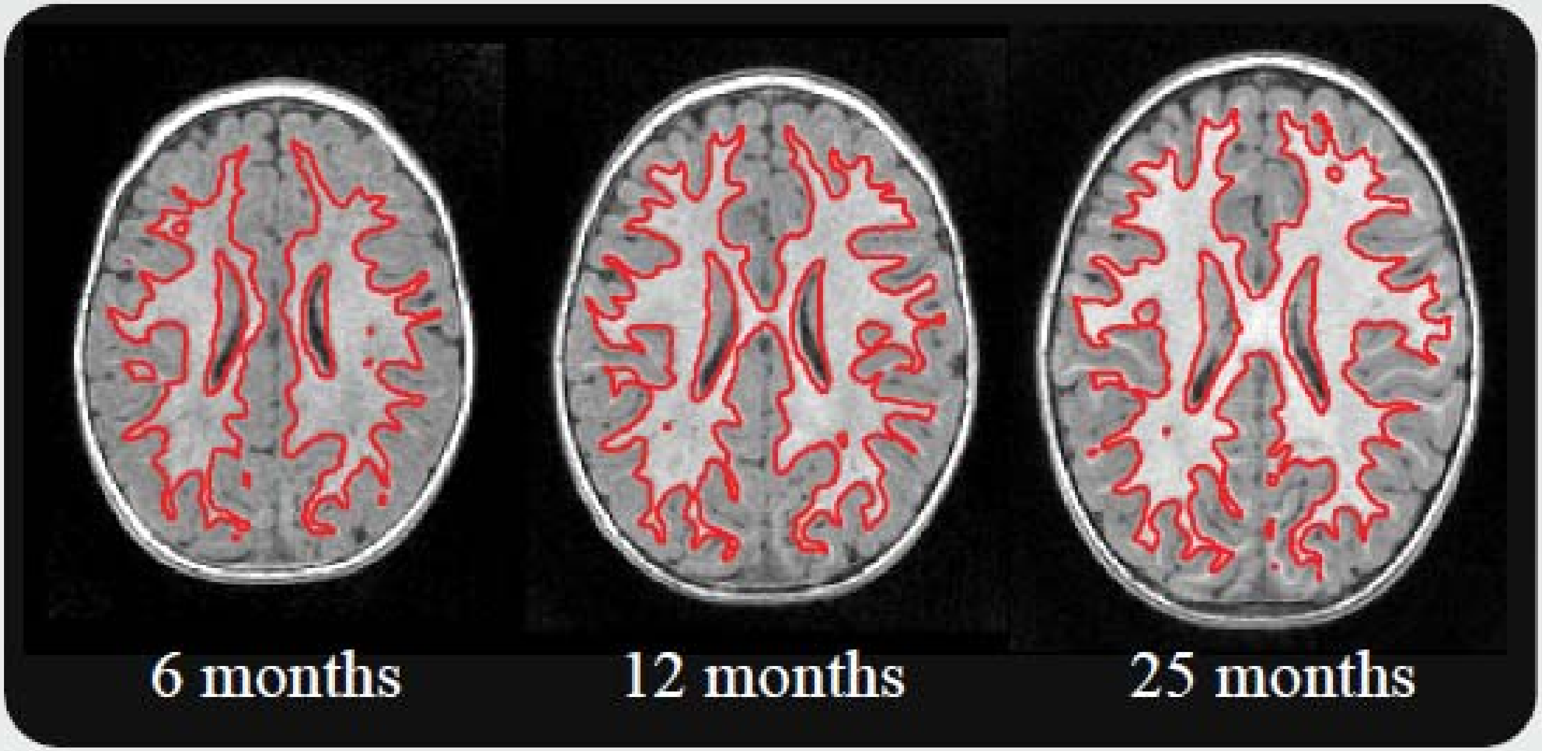
Geodesic Regression of Images + Shapes

$$E(\mathbf{S}_0, I_0, X_0) = \sum_{t_i} \Big(\underbrace{\lambda_{S_{t_i}} d_S(X(t_i), X_i)}_{\text{Image match (L2-norm)}} + \underbrace{\lambda_{I_{t_i}} d_I(I(t_i), I_i)}_{\text{Shape match (currents metric)}} \Big) + \underbrace{\mathrm{Reg}(\mathbf{S}_0)}_{\text{Regularity}}$$

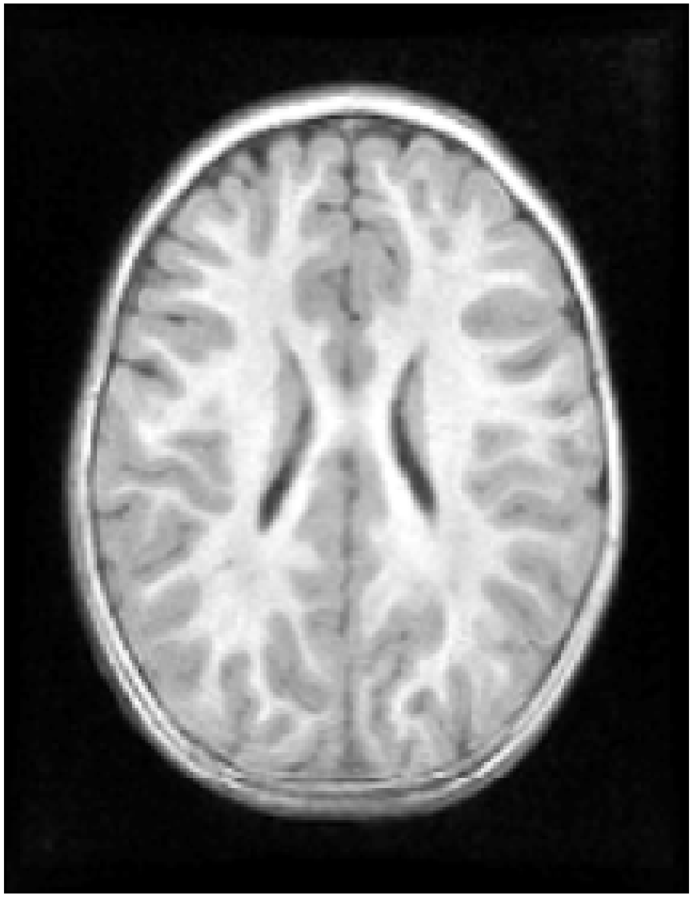


Pediatric Brain Development

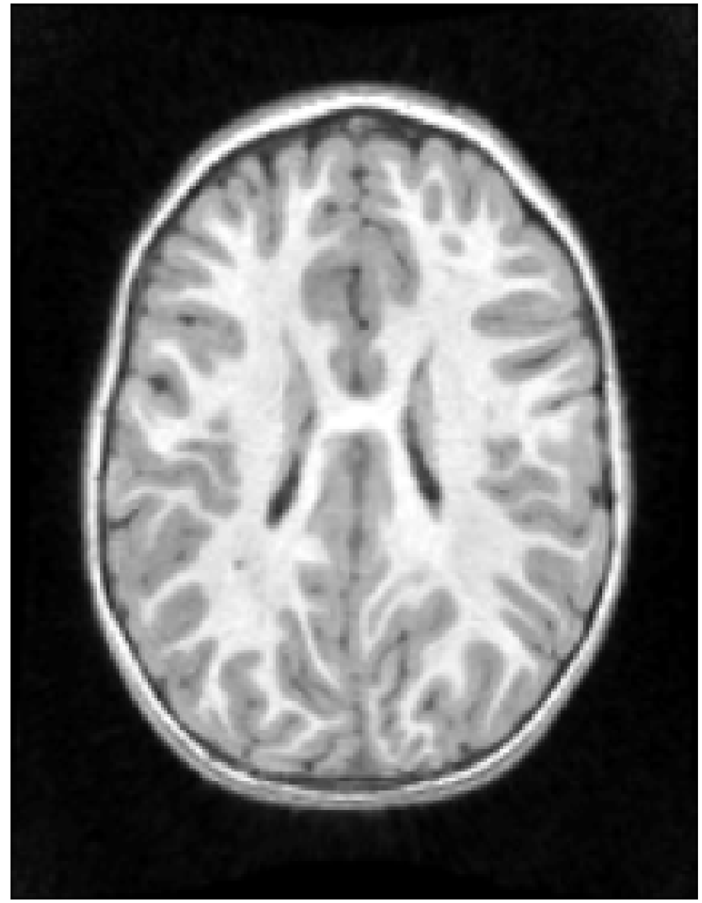


Longitudinal sequence of observed T1W images and white matter surfaces used for model estimation.

Pediatric Brain Development

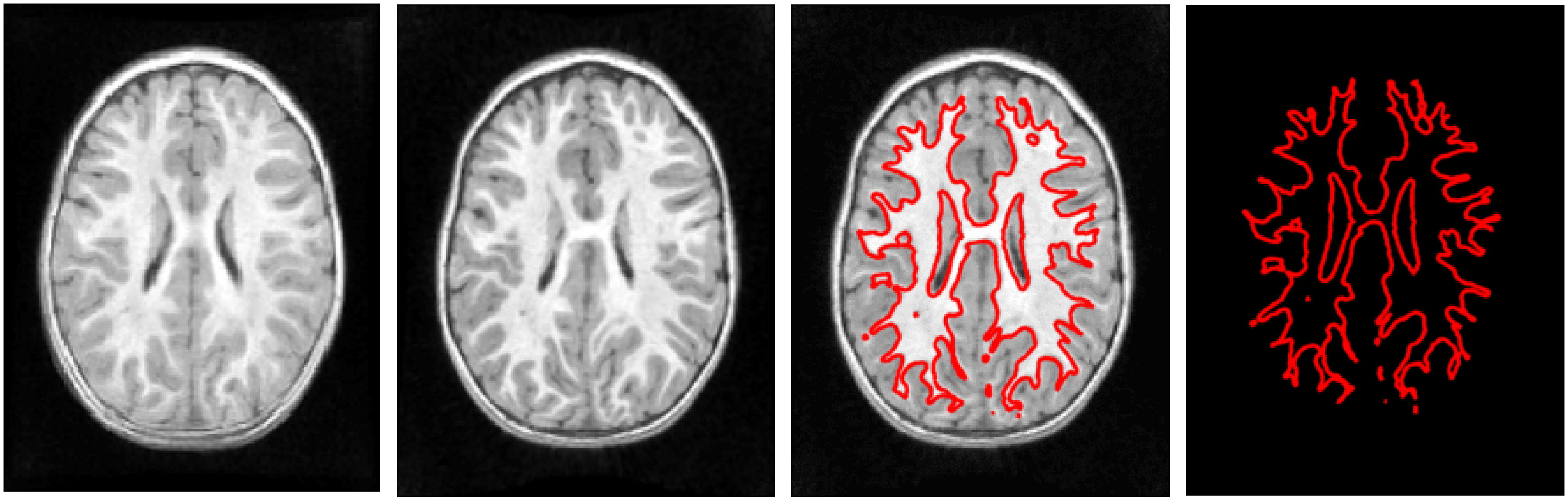


Estimation with images only



Estimation jointly but only showing image

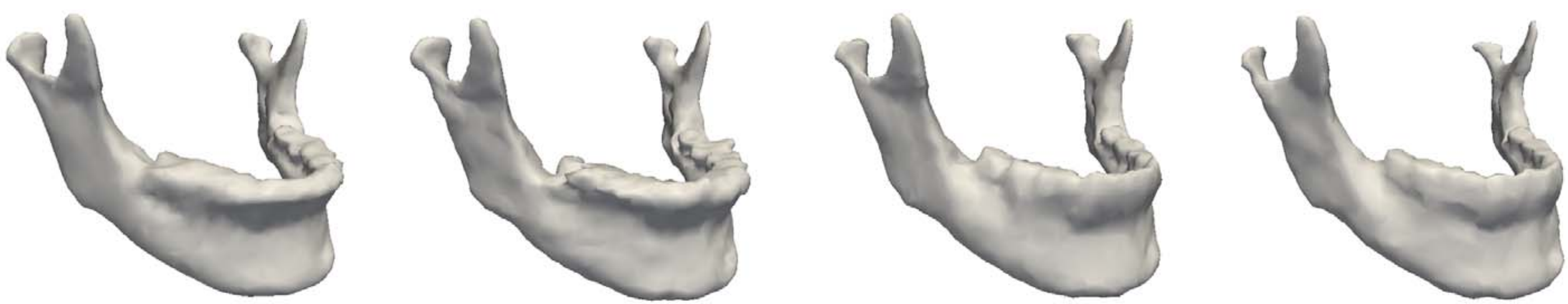
Pediatric Brain Development



1) Estimation with images only
2) Estimation jointly but only showing image
3) Estimation jointly and showing both image and white matter
4) Estimation with white matter surfaces only

Longitudinal Shape Modeling

Example mandibular surgery case (Prof. L. Cevidanes), 16-22 years post-surgery.

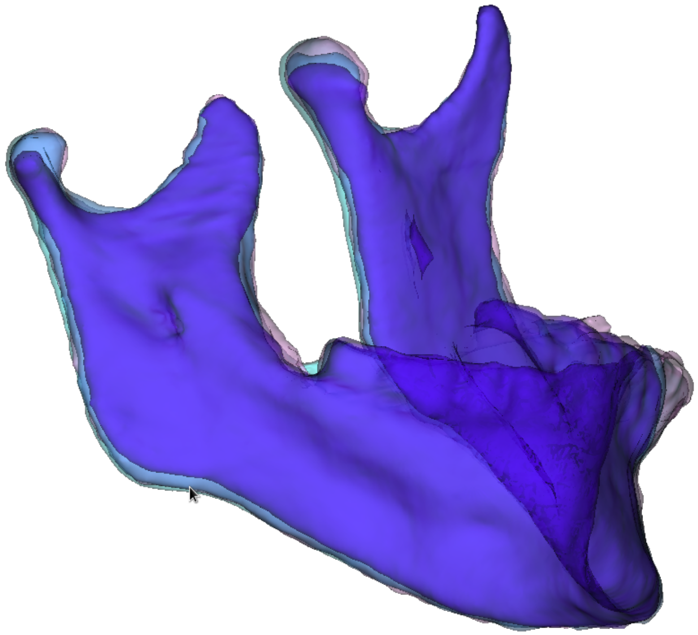


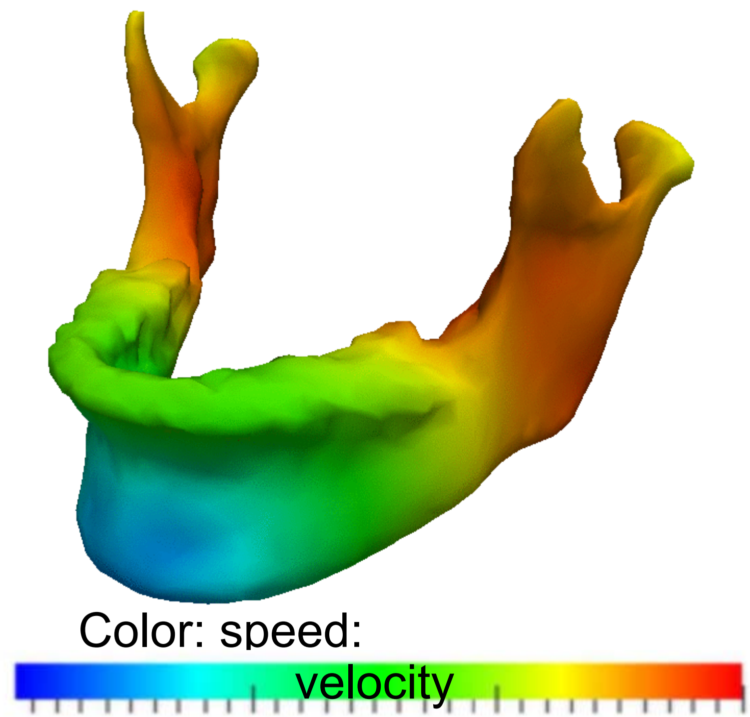
Follow-up scans in 2 years intervals.

Qualitative analysis from overlay: Do we understand remodeling after surgery?

Longitudinal Shape Modeling

Example mandibular surgery case (Prof. L. Cevidanes), 16-22 years post-surgery.





Qualitative analysis from overlay: Do we understand remodeling?

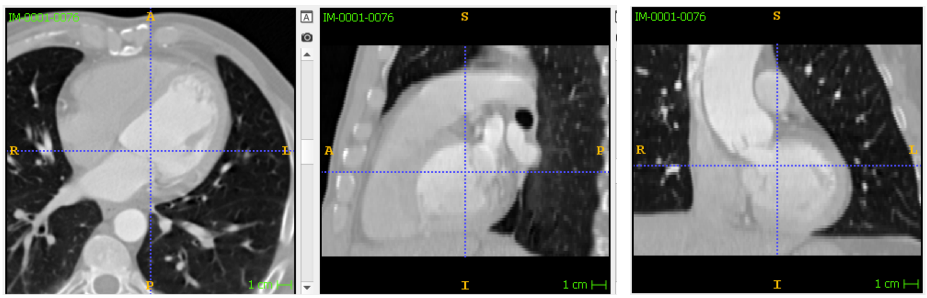
Spatio-temporal shape regression: Local and global.

Preliminary: 4D Heart Modeling

Data

Alias Name: MAGIX
Modality: CT 64
File Size: 69 MB
Description:
4D Cardiac CT.

10 volumes (512^2*76) across single heart cycle



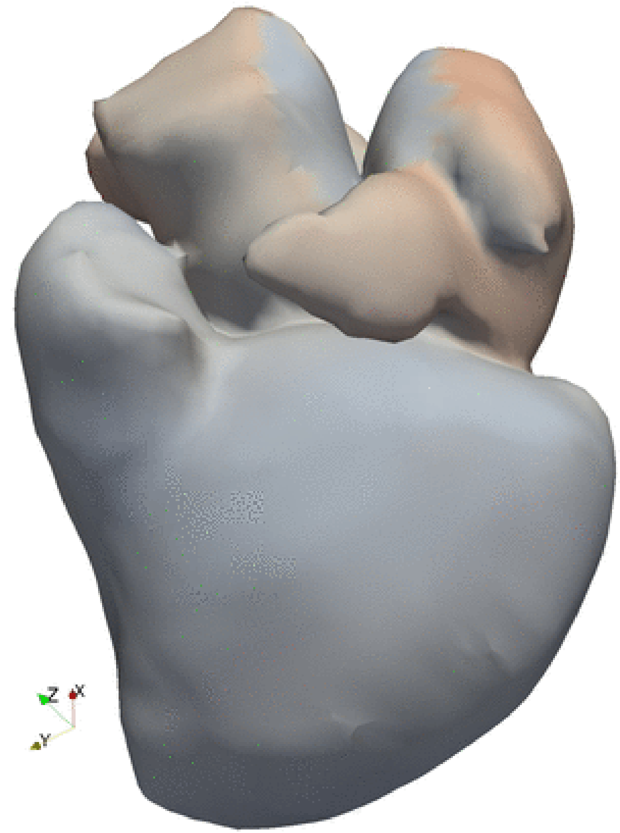
http://www.osirix-viewer.com/resources/dicom-image-library/

Segmentation

H.A. Kirisli, M. Schaap, S. Klein, S.L. Papadopoulou, M. Bonardi, C.H. Chen, A.C. Weustink, N.R. Mollet, E.J. Vonken, R.J. van der Geest, T. van Walsum, and W.J. Niessen, Medical Physics, vol. 37(12), pages 6279-6292, December 2010

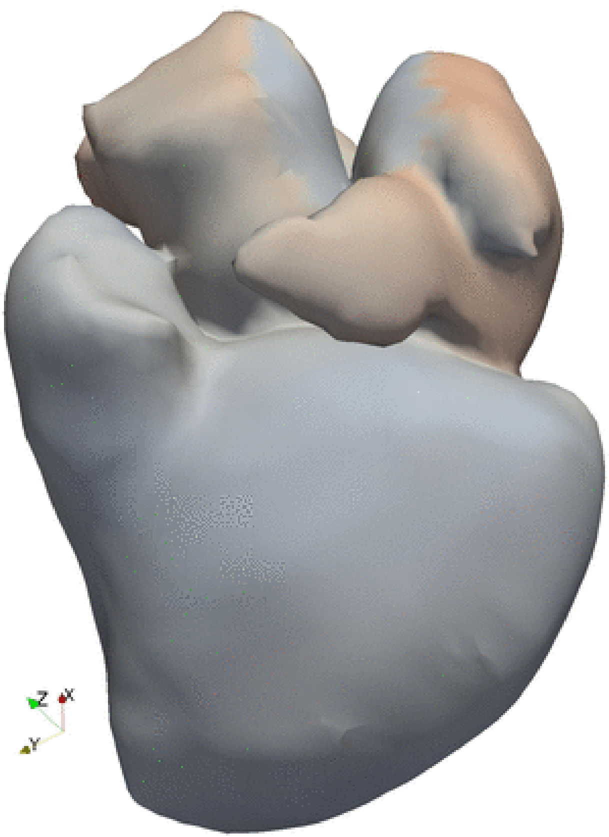
Preliminary: 4D Heart Modeling

Original segmented data, loop through 10 datasets

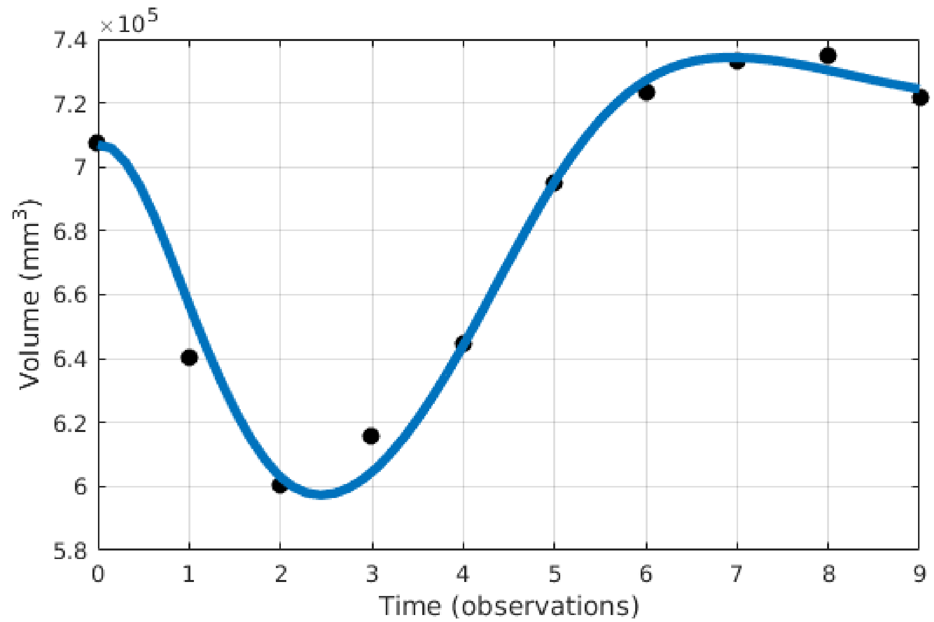


Regression: Blue/red: contraction/expansion

Preliminary: 4D Heart Modeling

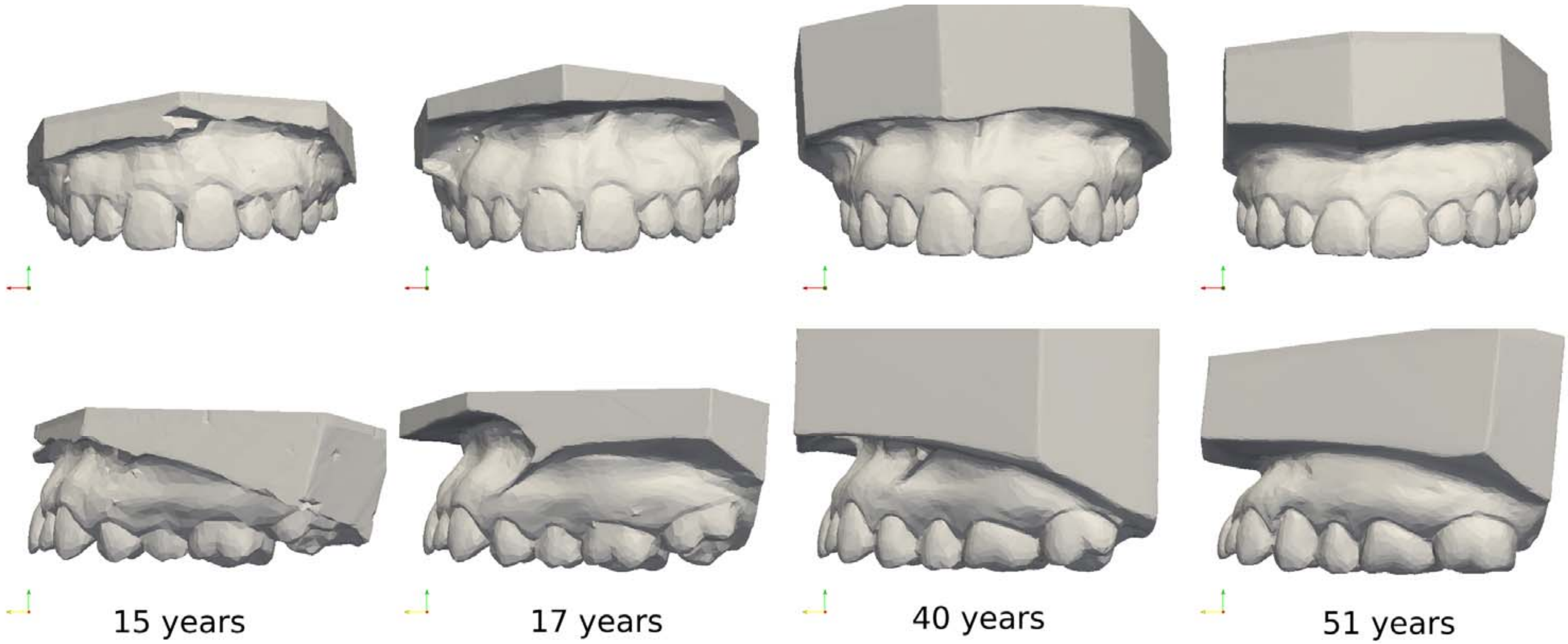


Regression: Blue/red: contraction/expansion



Volumes: Original versus 4D regression model

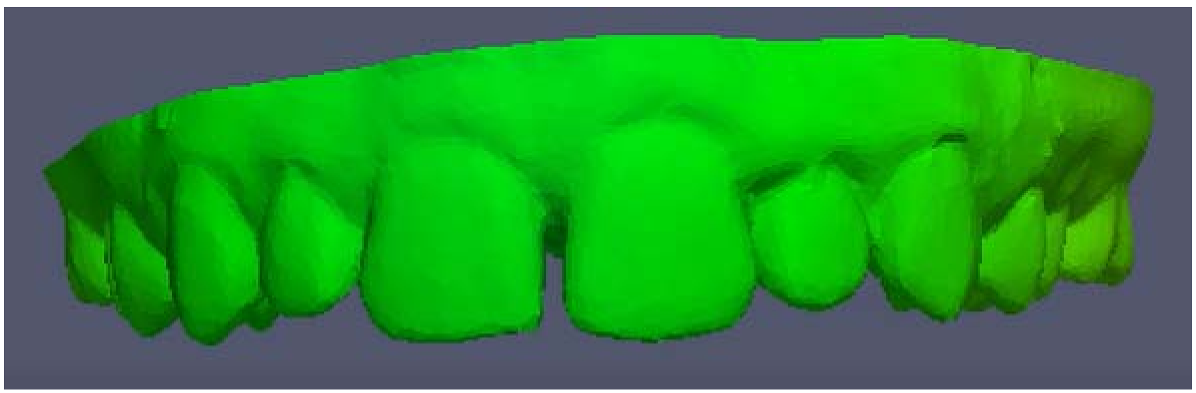
Dental Surgery (L. Cevidanes et al.)



- Model of aging changes in the dental arches.
- 6 time points of upper dental arches of single subject at ages 11, 13, 15, 17, 42 and 52.

Dental Surgery (L. Cevidanes et al.)

- 4D spatio-temporal shape regression can be used to generate a model of aging changes in the dental arches



- Sample case: normal dental arch
- Future goal: extend analysis to patients with cleft alveolus and palate.

Contents

- Towards Longitudinal Atlas ▶
- 4D Shape Analysis ▶
- Clinical applications:
  - Autism Research ▶
  - Huntington's Disease (HD) ▶
  - Glaucoma Research ▶
- Conclusions

Driving Motivation: Autism

Complex neurodevelopmental disorder.

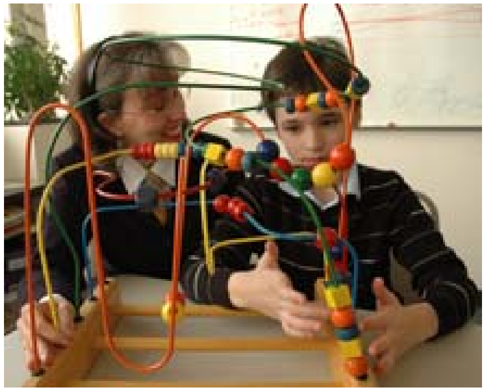
Many subjects require long-term care and costly therapy.

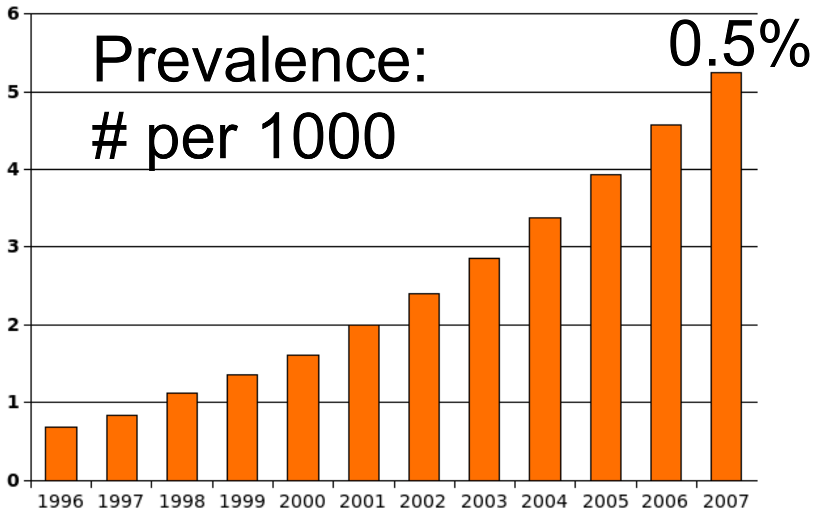
Reports of autism cases per 1,000 children grew dramatically in the U.S. from 1996 to 2007.

Prevention?

Treatment?

The earlier intervention starts, the better the outcome





Recent statistics: 1 in 68 (1.5%)

Research: Studies of early brain development:

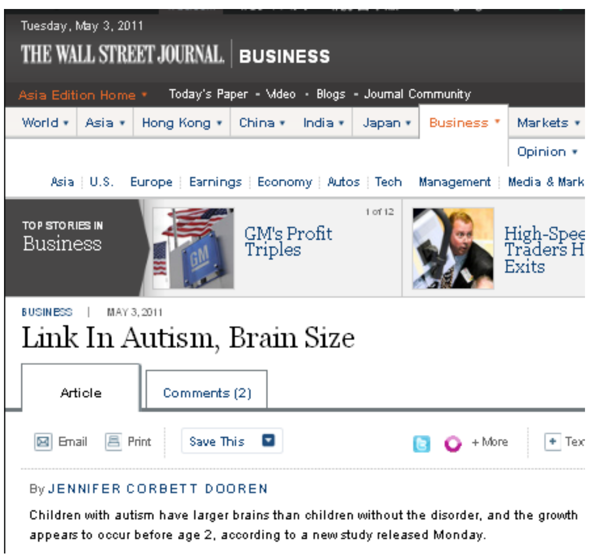
- **Theory of cause and of brain alterations**
- **Timing and onset**
- **Hope: Better, earlier therapy**

Autism Spectrum Disorder (ASD)

SIMONS FOUNDATION Send to printer

Brain expands too fast, shrinks too soon in autism

Brain drain: Overall brain volume decreases and the cortex thins at a faster-than-normal rate in young adults with autism.


Tuesday, May 3, 2011

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BUSINESS | MAY 3, 2011

Link In Autism, Brain Size

Article | Comments (2)

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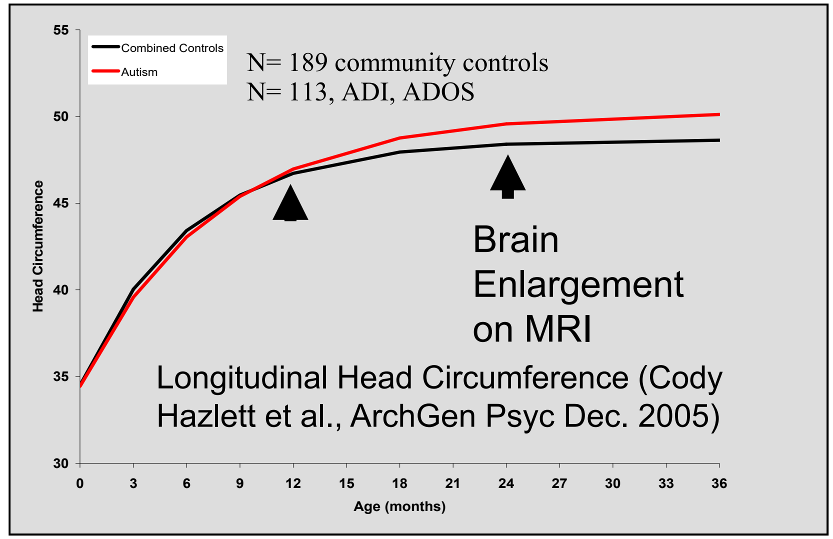
By JENNIFER CORBETT DOOREN

Children with autism have larger brains than children without the disorder, and the growth appears to occur before age 2, according to a new study released Monday.

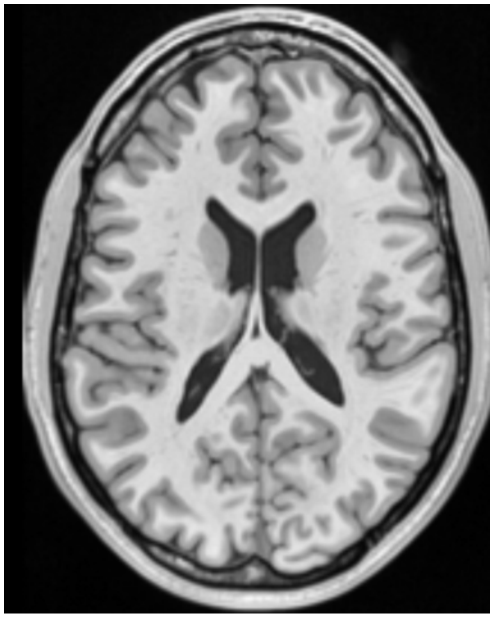
Arch Gen Psychiatry. 2011;68(5):467-476

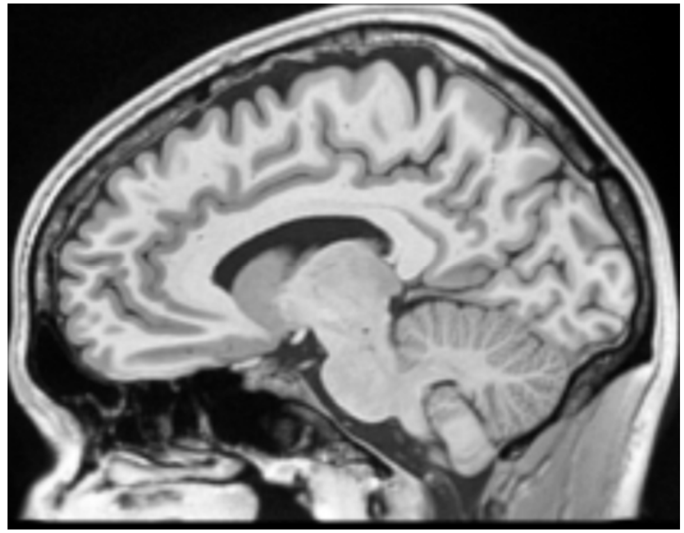


Early Finding:

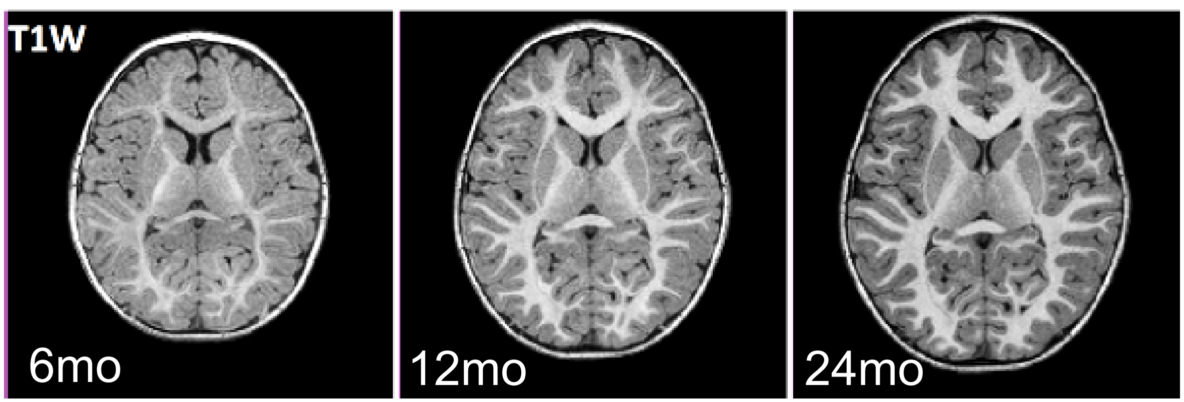
- Brain enlargement in autism seems to start at year 1 or earlier
- Why? What? Effect?
- Better understanding → Early intervention to improve outcome
- **What measurements to use?**

Magnetic Resonance Imaging (MRI)



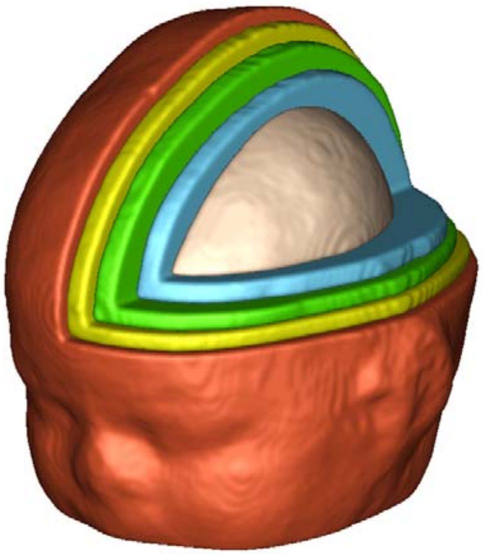


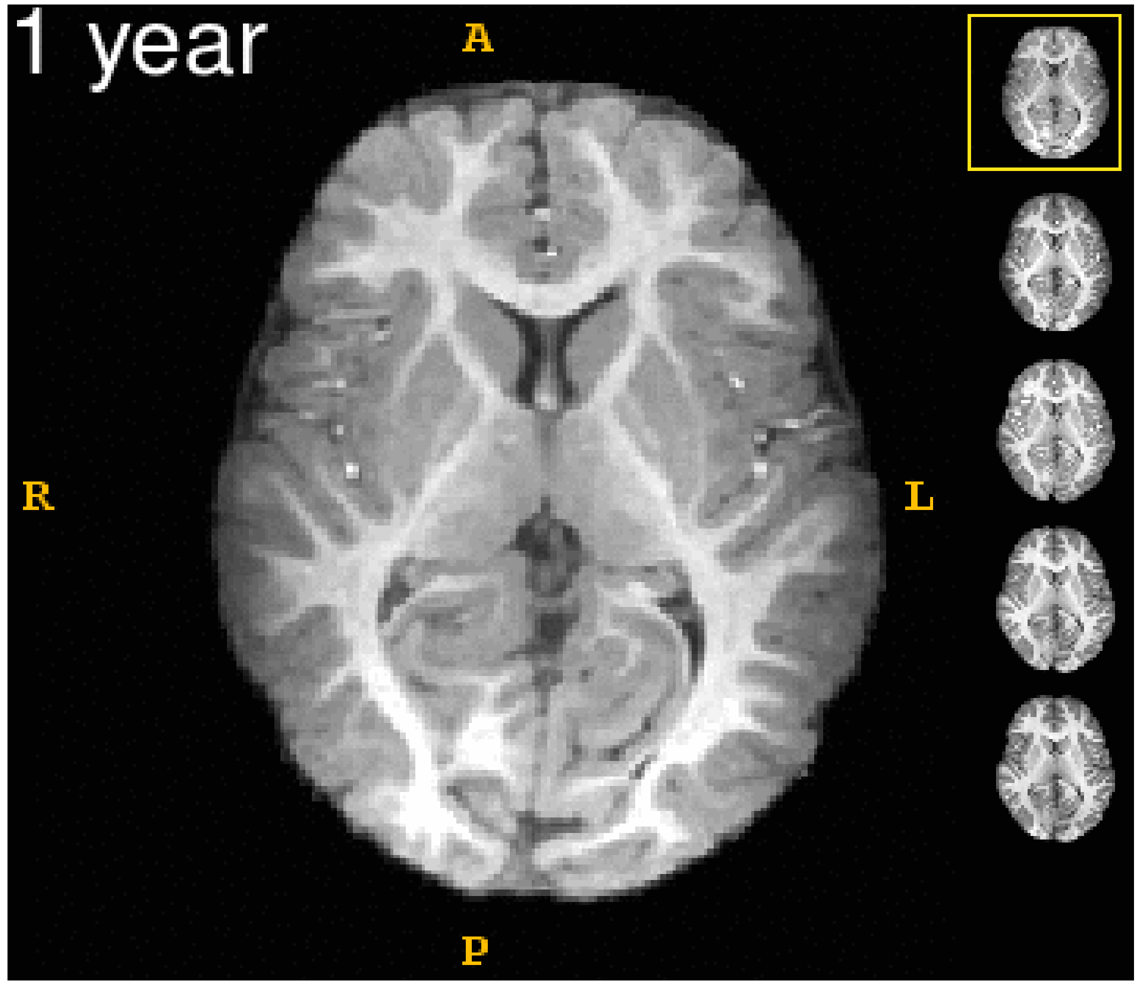
Non-invasive, quick, 3D comfortable scanning (10Min)



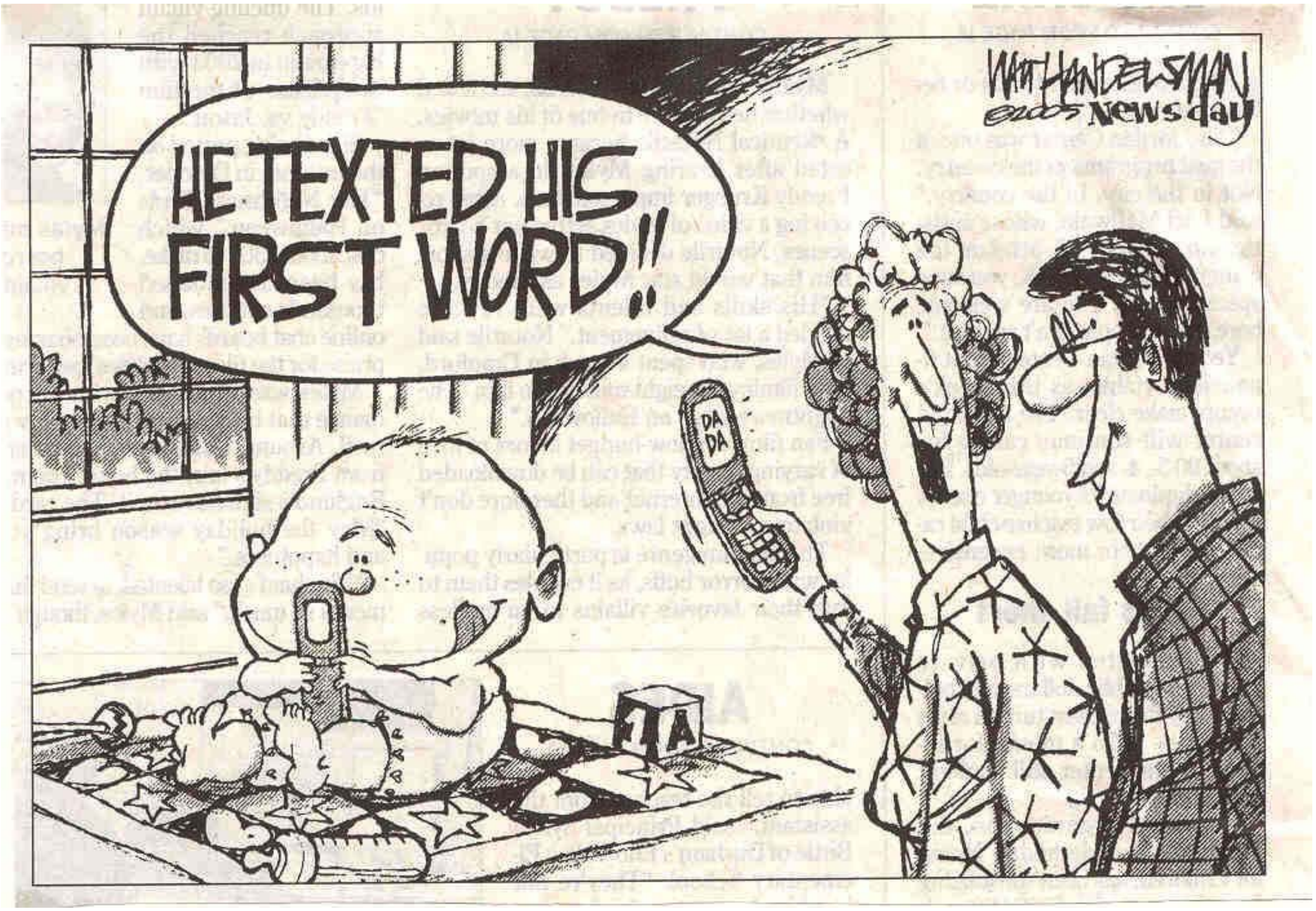
Study of Growth: Longitudinal Infant Scans (6 to 24 months)

Subject-specific longitudinal MRI



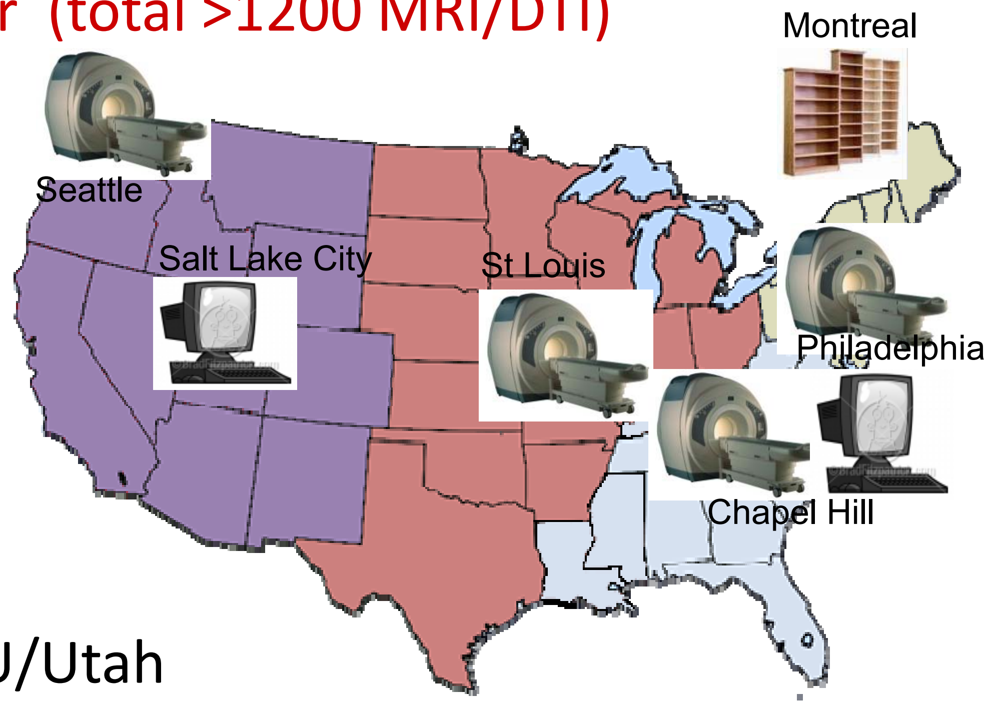


Understanding early Development …

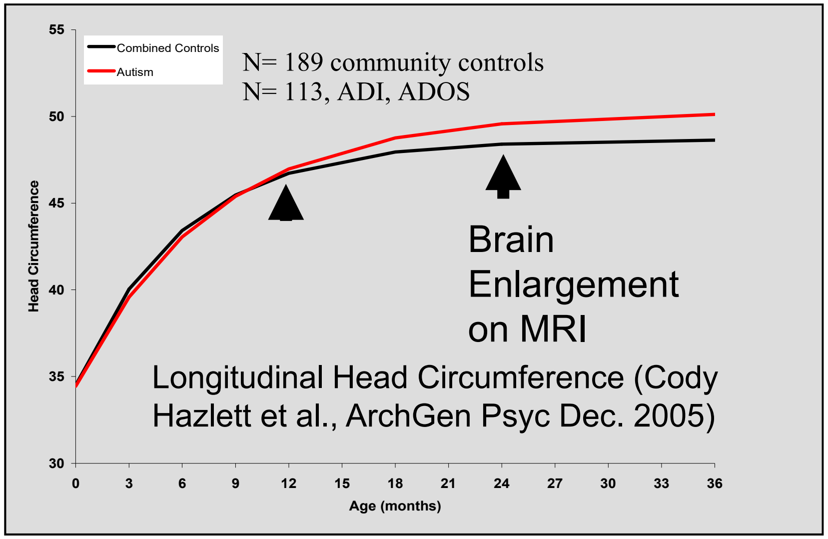


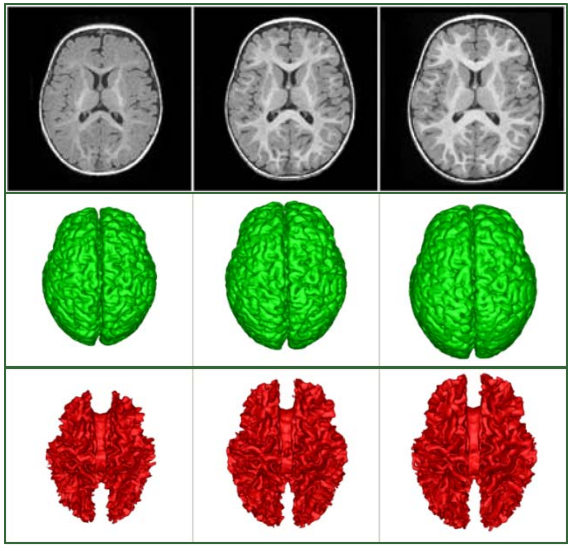
ACE-IBIS: **A**utism **C**enters of **E**xcellence Infant Brain Imaging Study

- P.I. Joseph Piven, UNC
- Longitudinal study of infant siblings at risk for Autism scanned at 6mo, 1y and 2yr (total >1200 MRI/DTI)
- 4 scanning sites:
  - Seattle (2 scanners)
  - St. Louis
  - Philadelphia
  - Chapel Hill (2 scanners)
- DCC: MNI Montreal
- Image analysis: UNC & NYU/Utah

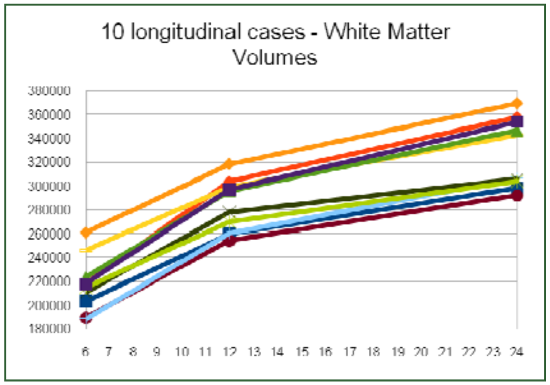


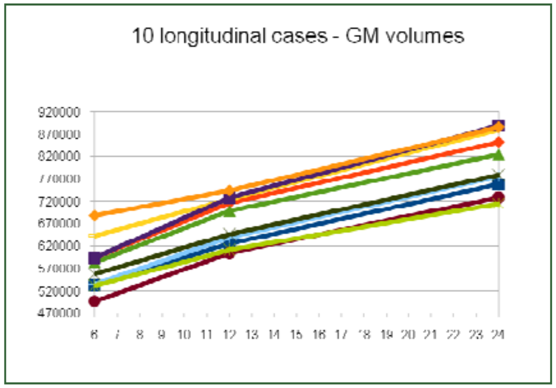
Goal: Growth Trajectories





Quantitative analysis of subject-specific trajectories



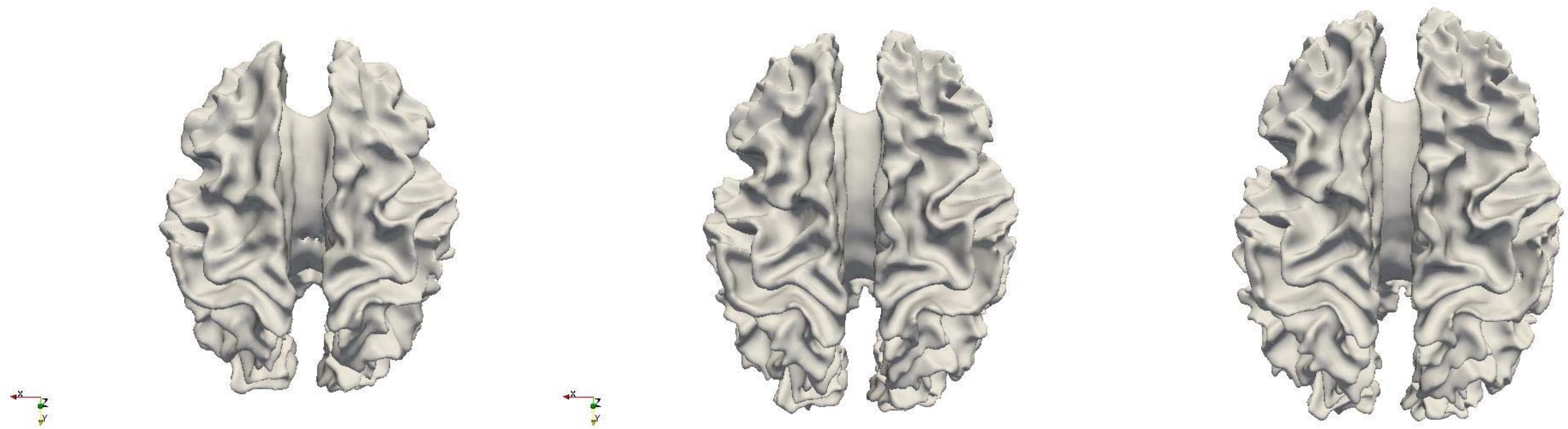


Mixed effects modeling:

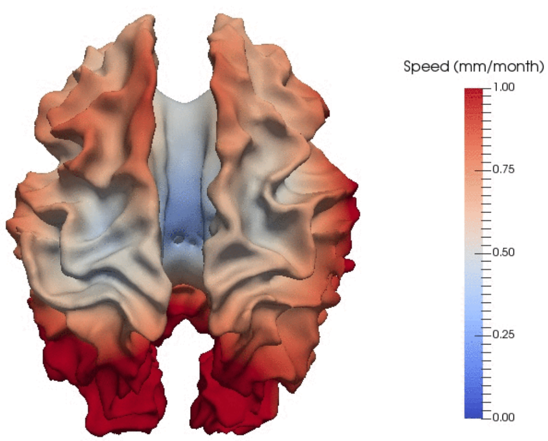
- Fixed effects
- Random effects

Variation btw individuals versus subtle changes over time

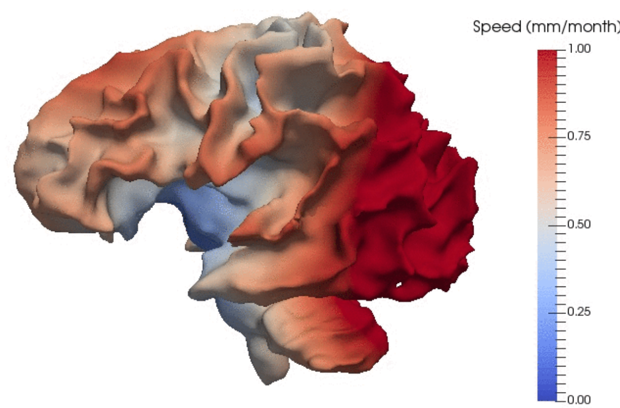
Early Brain Development: 4D Shape Trajectories



6 month 12 month 24 month



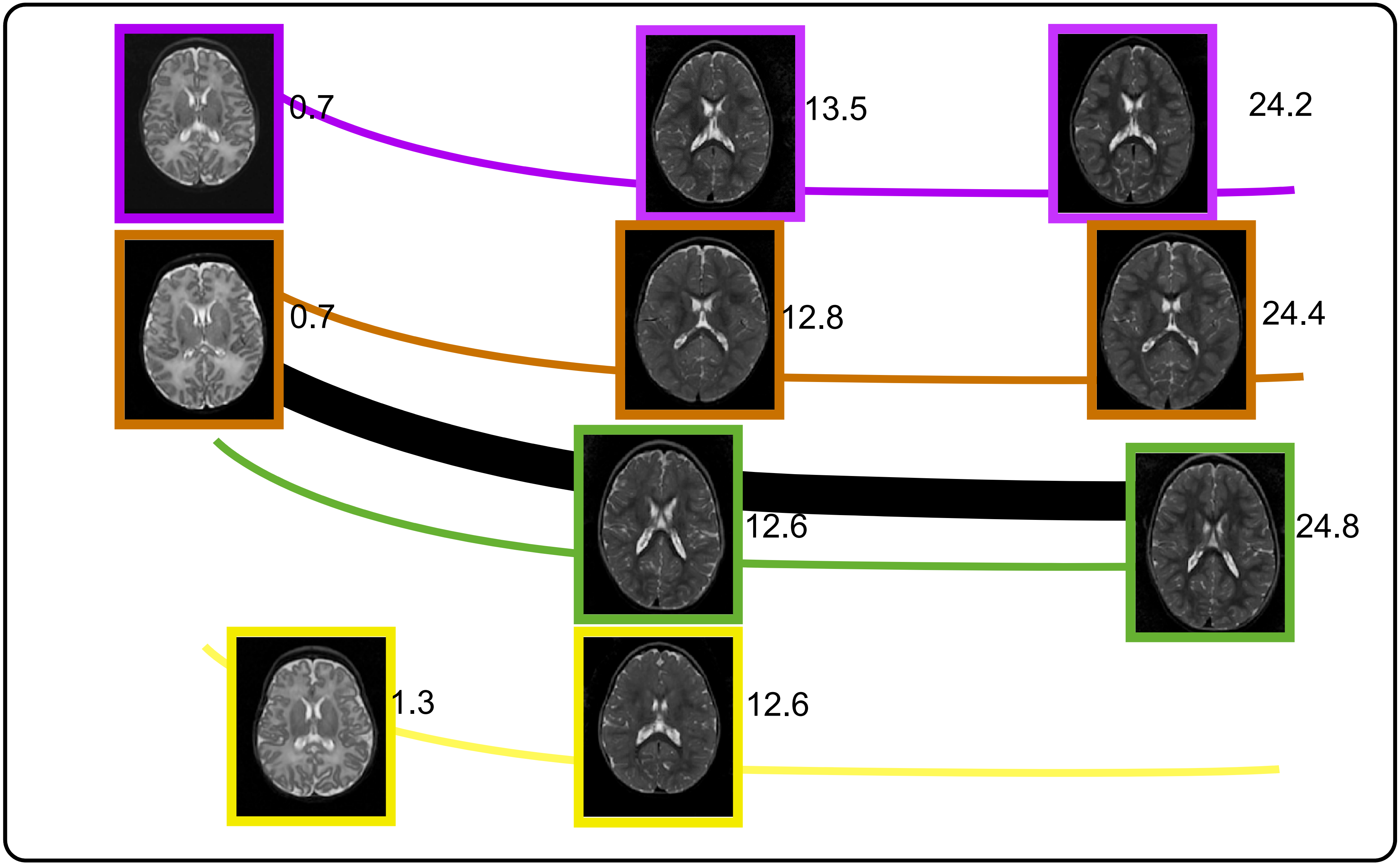
6.00 months



6.00 months

Geodesic Image Regression: Fishbaugh, Durrleman et al., 2015 / 2017

Why is continuous regression important?



nature

LETTER

doi:10.1038/nature21369

Early brain development in infants at high risk for autism spectrum disorder

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Autism detectable in brain long before symptoms appear

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NEWS

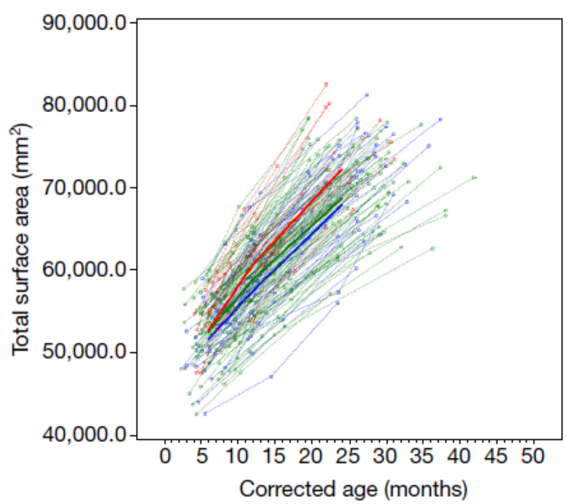
Brain scans can detect autism long before any symptoms start to emerge, say scientists.

LETTER

doi:10.1038/nature21369

Early brain development in infants at high risk for autism spectrum disorder

- 106 high risk, 42 low risk infants, MRI at 6/12/24 months.
- Hyperexpansion of cortical surface area between 6 and 12 months precedes brain volume overgrowth btw 12 and 24.
- Deep-learning algorithm that uses **surface area** from MRI of the brain of **6–12-month-olds predicted the diagnosis of autism** in individual high-risk children at 24 months (81% positive predictive value, 88% sensitivity).



Autism detectable in brain long before symptoms appear

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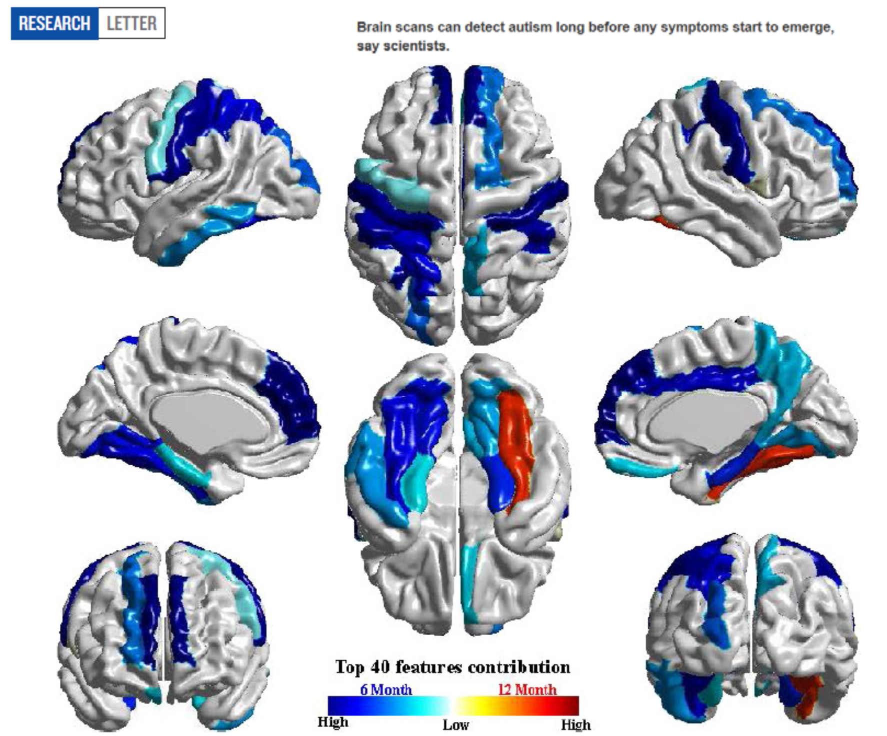
NEWS

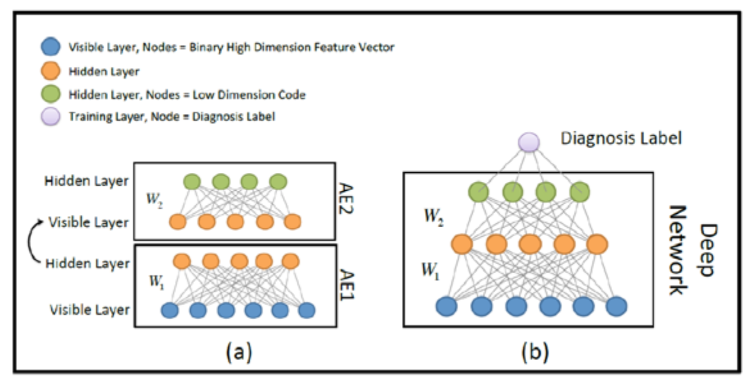
Brain scans can detect autism long before any symptoms start to emerge, say scientists.



Extended Data Figure 1 | Visualization of cortical regions with surface area measurements among the top 40 features contributing to the linear sparse learning classification. The cortical features produced by the deep learning approach (Fig. 3) are highly consistent with those observed using an alternative approach (linear sparse learning) shown here. Results from this alternative approach are included for comparison in Supplementary Tables 2 and 3.

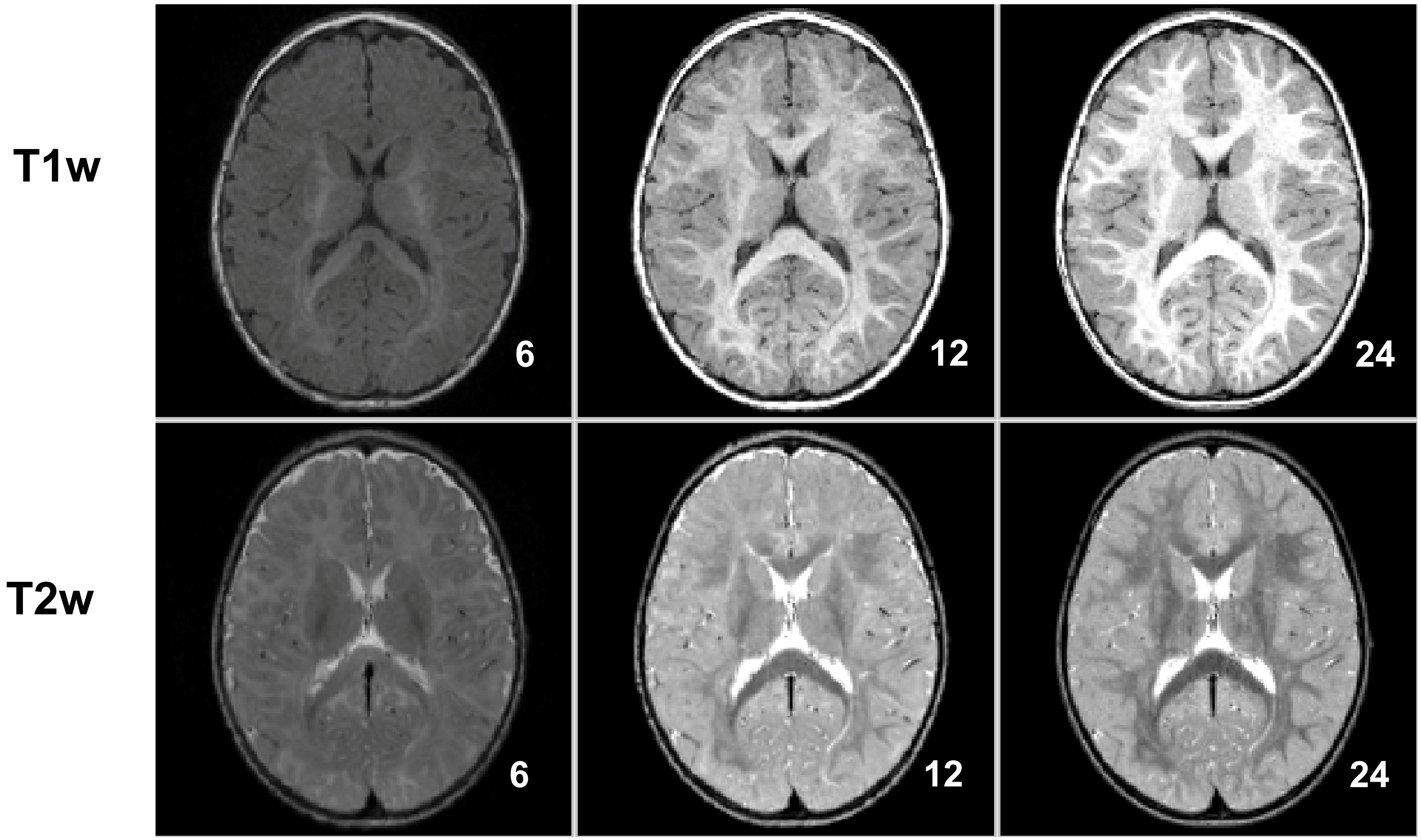
Role of Deep Learning

- **Data**: MRIs, parcellated into 78 regions, (AAL) with brain volume, surface area, cortical thickness at 6 and 12 months of age, and sex of the infants.
- **Conventional** statistical analysis: PCA or Sparse Learning+SVM: No group differences
- **Deep learning**: Infers complex nonlinear relationships, 2-stage design, significantly outperformed other classification schemes



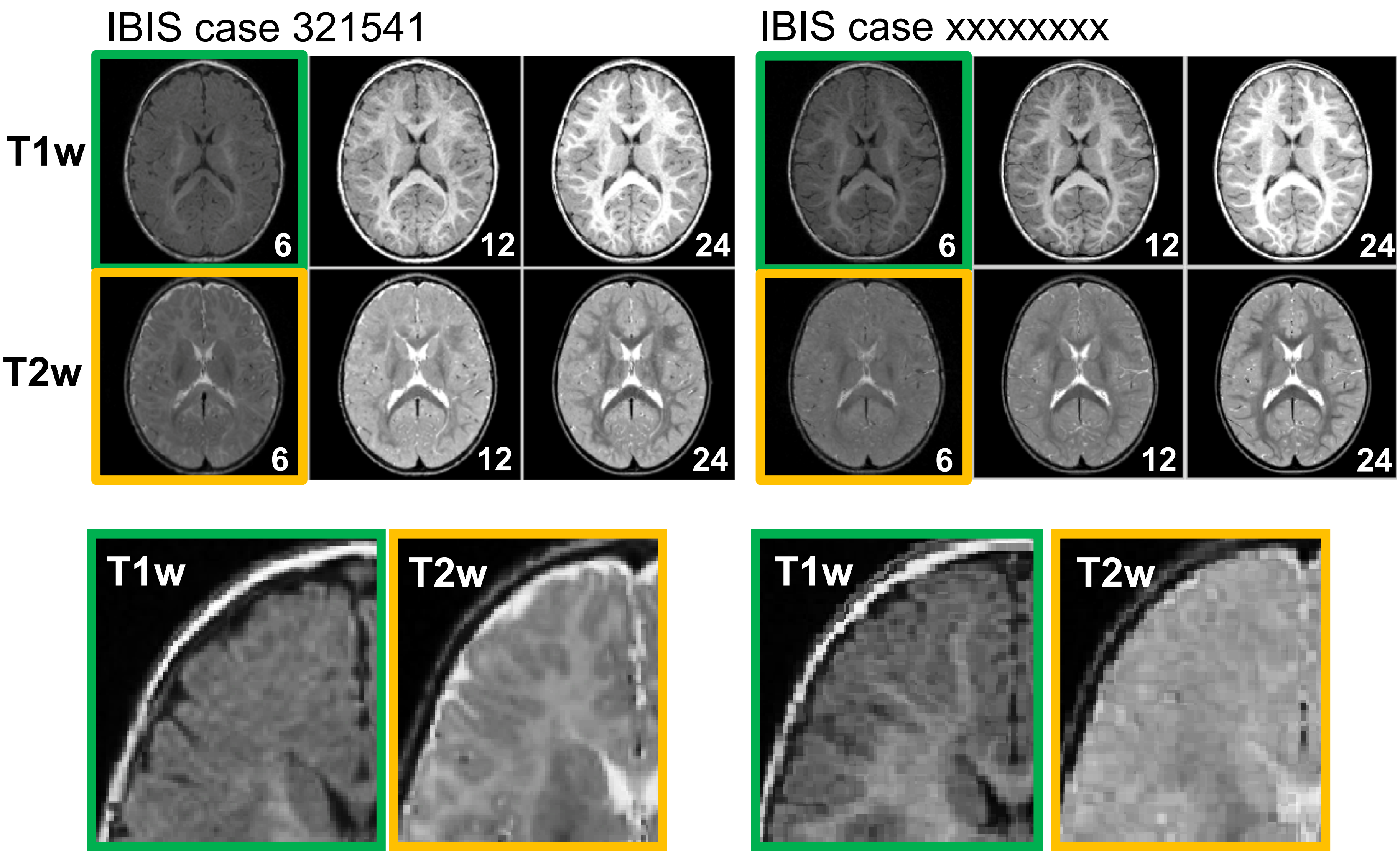
Motivation: Maturation seems encoded in multi-modal MRI contrast

Infant MRI

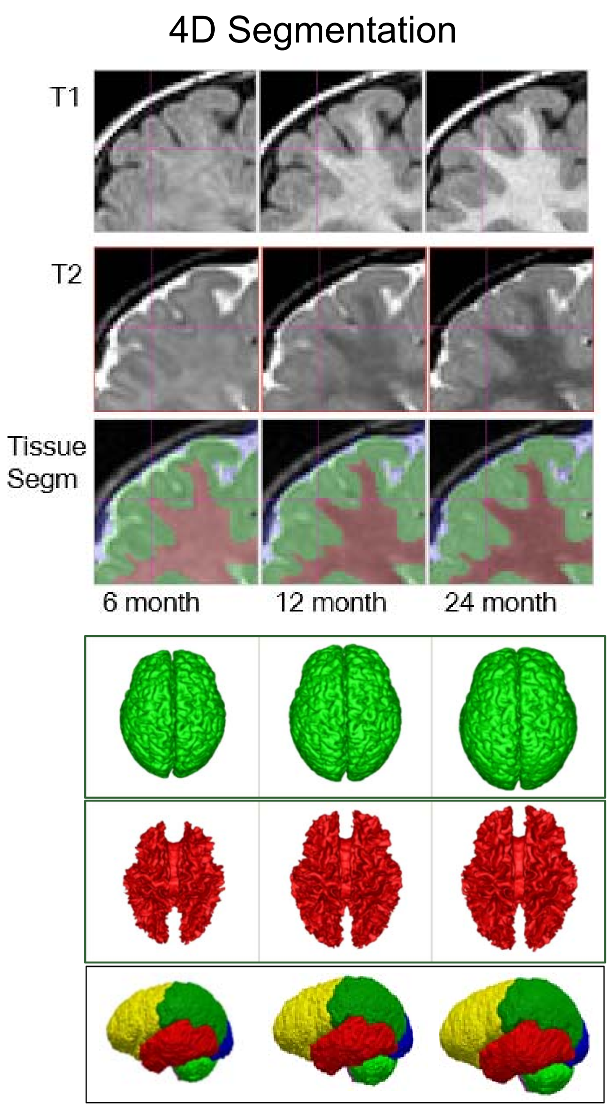


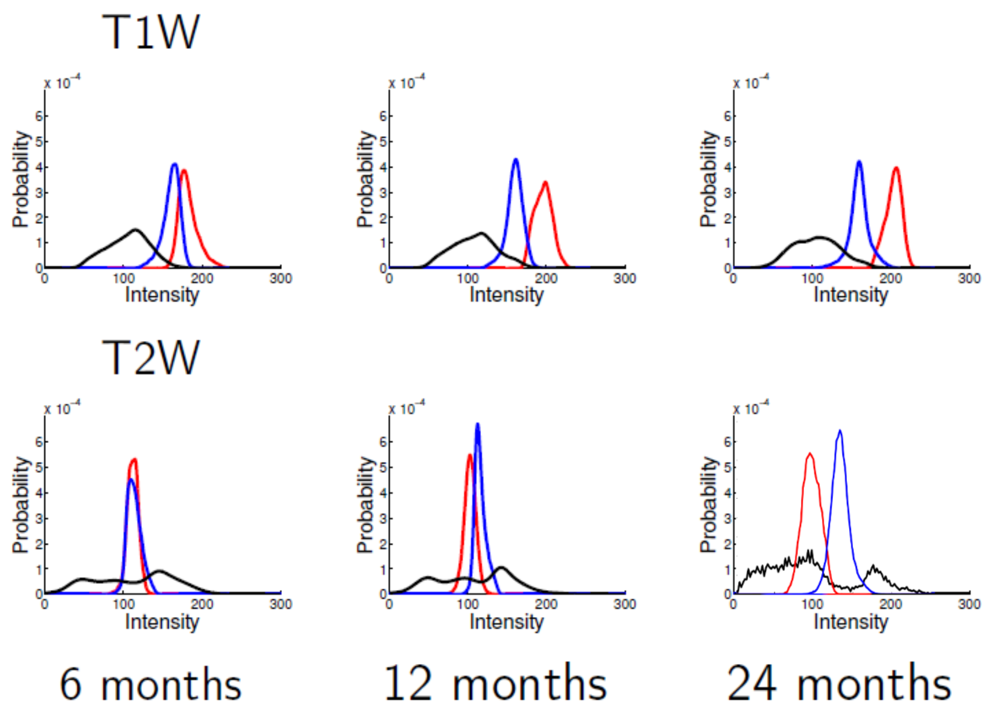
Vardha et al., MICCAI 2017

Motivation: Maturation seems encoded in multi-modal MRI contrast



Tissue Histograms in T1w & T2w by Age

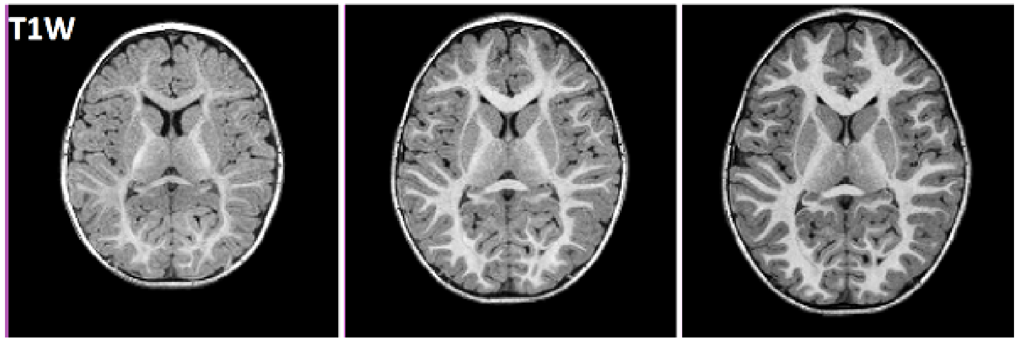


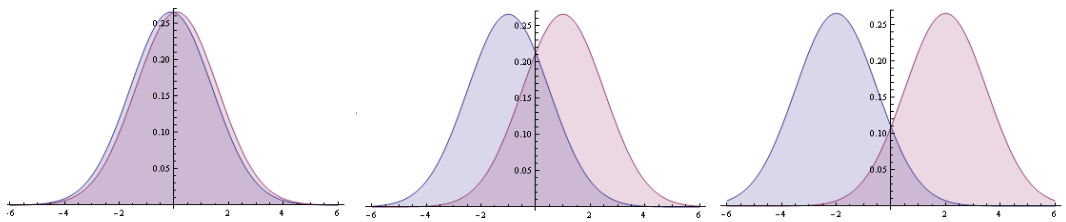


GM (blue), WM (red), CSF (black) intensity histograms

Avantika Vardhan et al., MICCAI'17, MICCAI '14, SPIE '14, ISBI '13

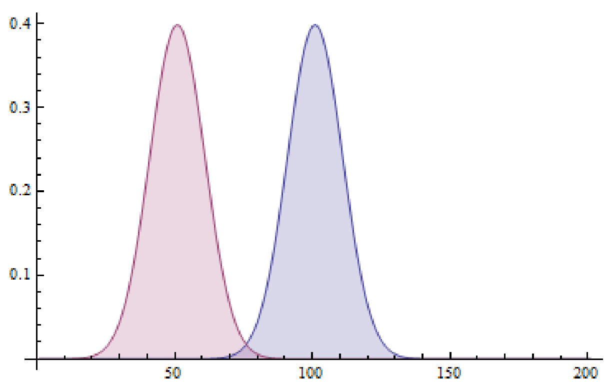
Model: WM/GM Contrast

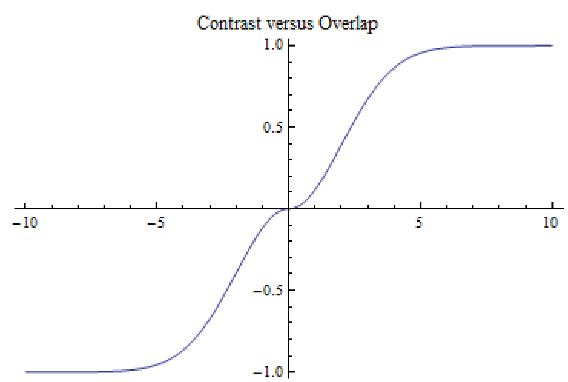




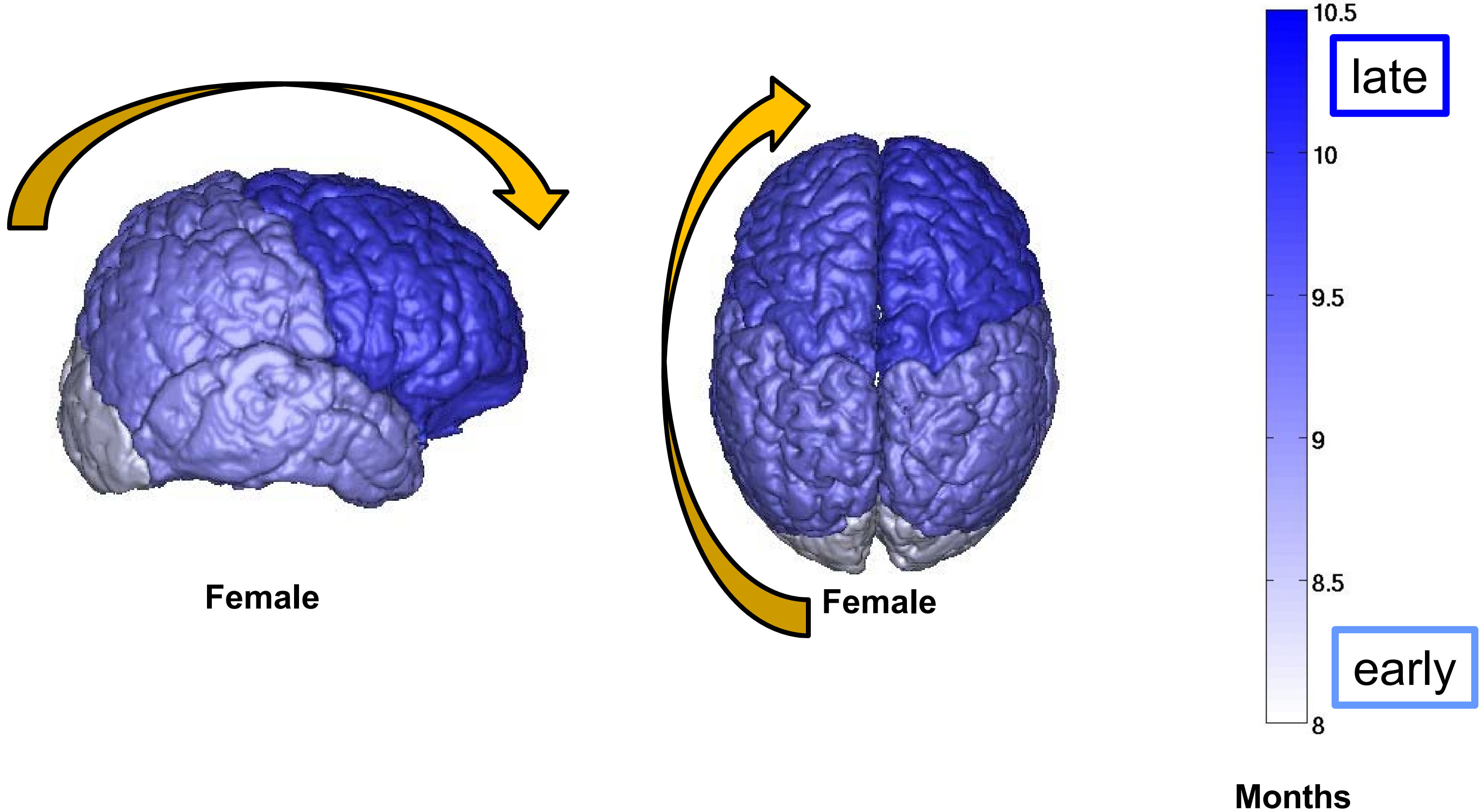
Measure of difference: “Overlap” of wm and gm distributions via Hellinger Distance metric:

$$HD(P1, P2) = \sqrt{2\left(1 - \int_y \sqrt{P1(y)P2(y)}dy\right)}.$$





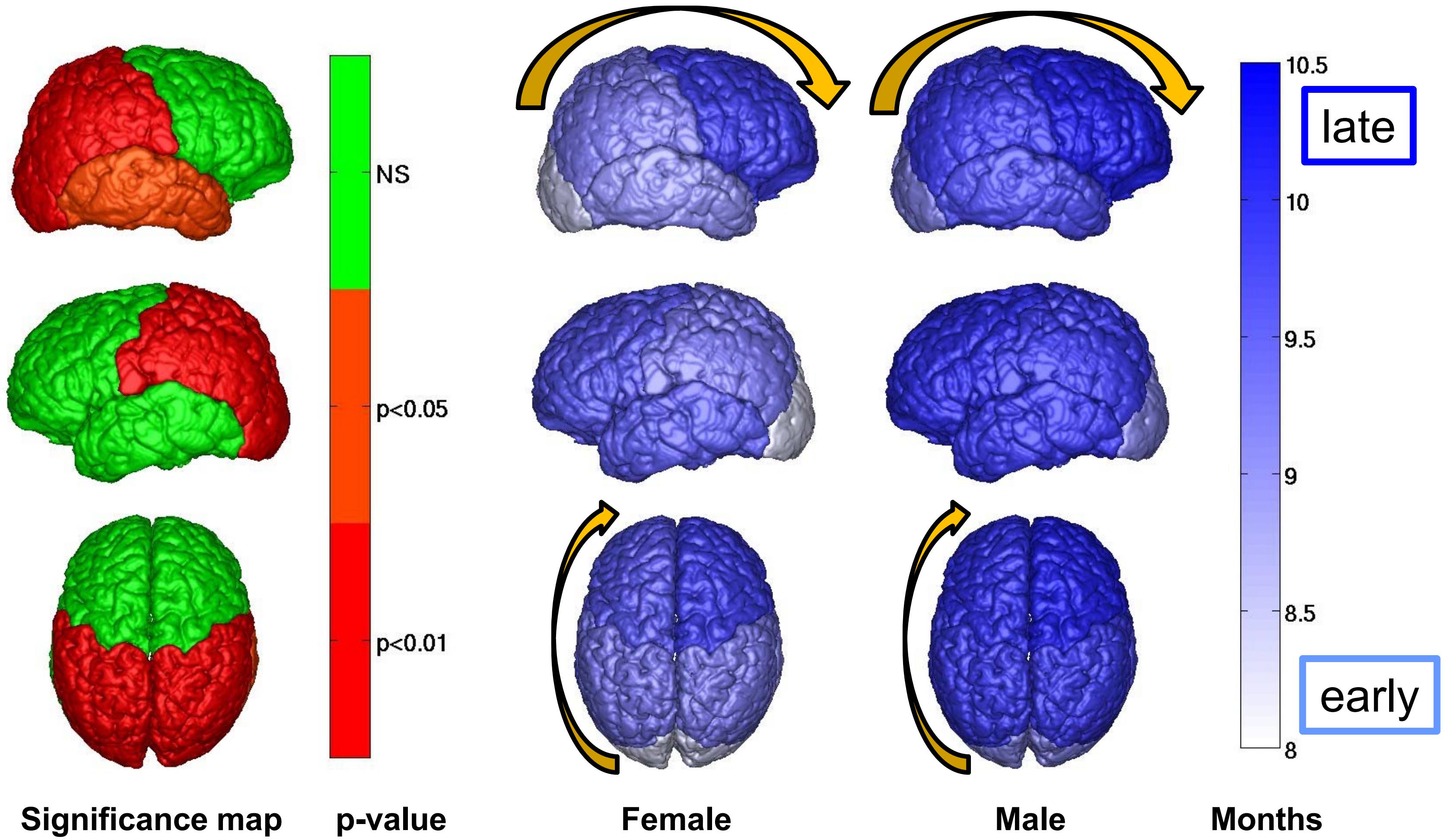
New Discovery: Pattern of Maturation



- Posterior – anterior pattern of timing of maturation
- Logistic modeling: Time at inflection point
- 24 Females, 46 Males, 3 timepoints 6/12/24 months

Vardha et al., MICCAI 2017

Sex Differences of Maturation



- Posterior → Anterior pattern of maturation
- Females earlier than males (9 to 23 days)

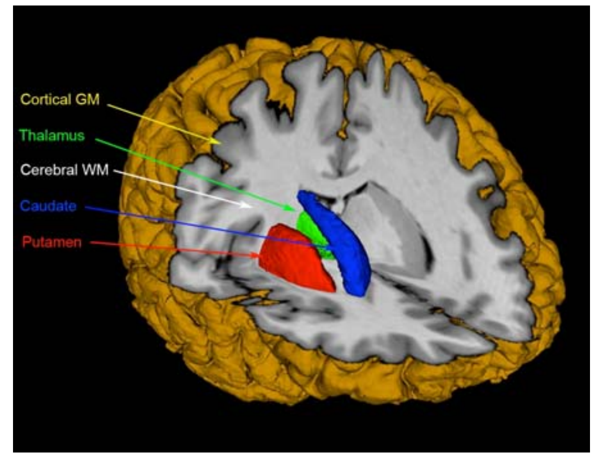
Vardha et al., MICCAI 2017

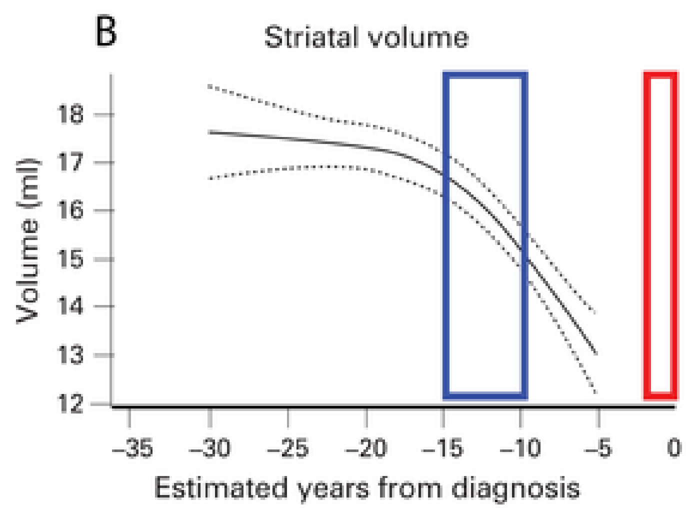
Contents

PREDICT-HD

Huntington's Disease: Search for noninvasive imaging biomarkers

- Symptomatic HD imaging findings
  - Atrophied caudate and putamen
  - Disproportionate loss of white matter
- Prodromal HD imaging findings
  - Striatal atrophy correlates with:
    - Neurological impairment
    - Poorer cognitive performance
    - Years to motor symptom onset
- How can we help HD patients?
  - Present: Symptomatic treatment (**no cure**)
  - Future: **Treatment** for **pre-symptomatic HD patients**

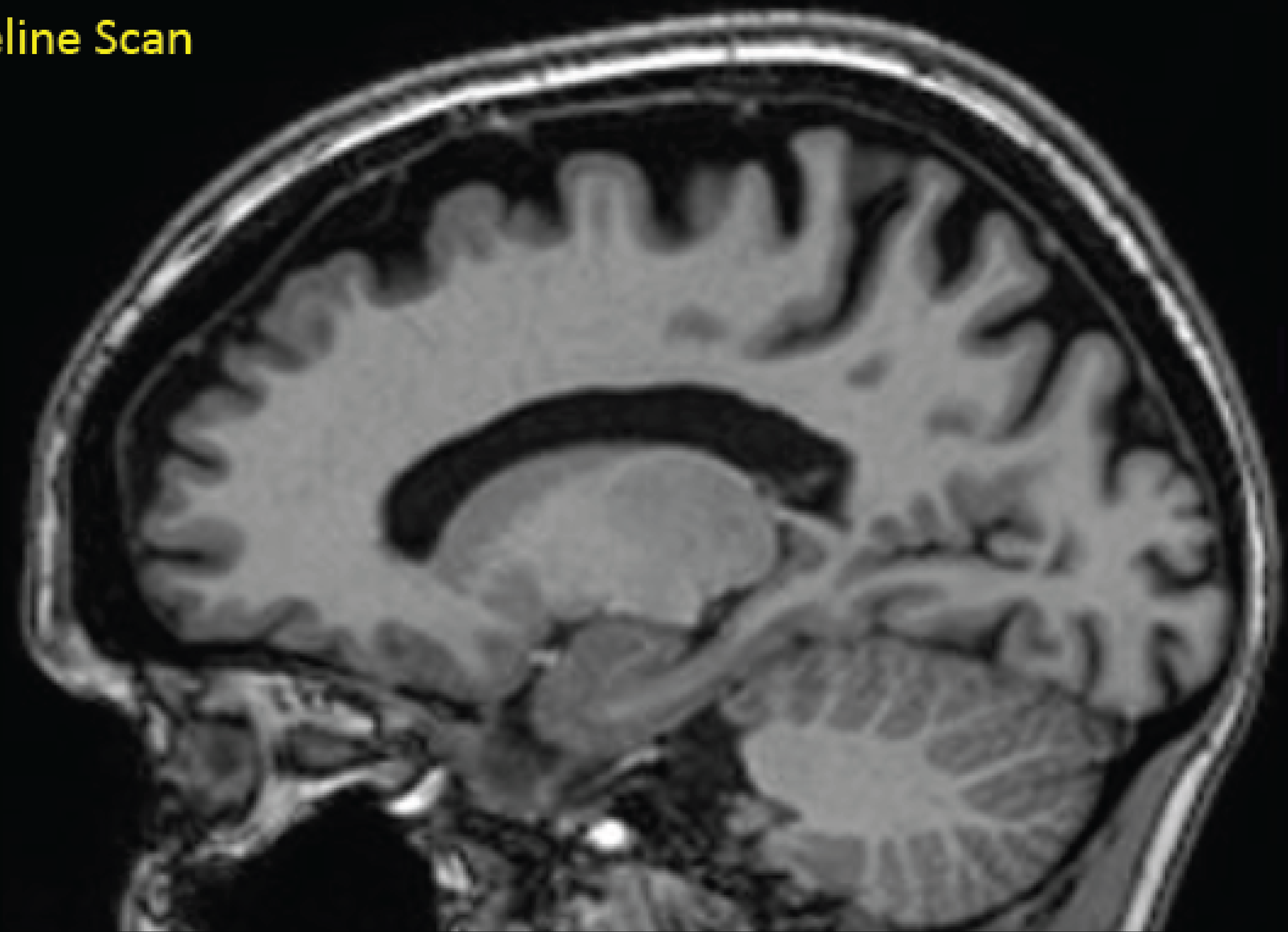




Courtesy Jane Paulsen, Hans Johnson, U-Iowa

TRACK-HD Stage 1 HD Subject

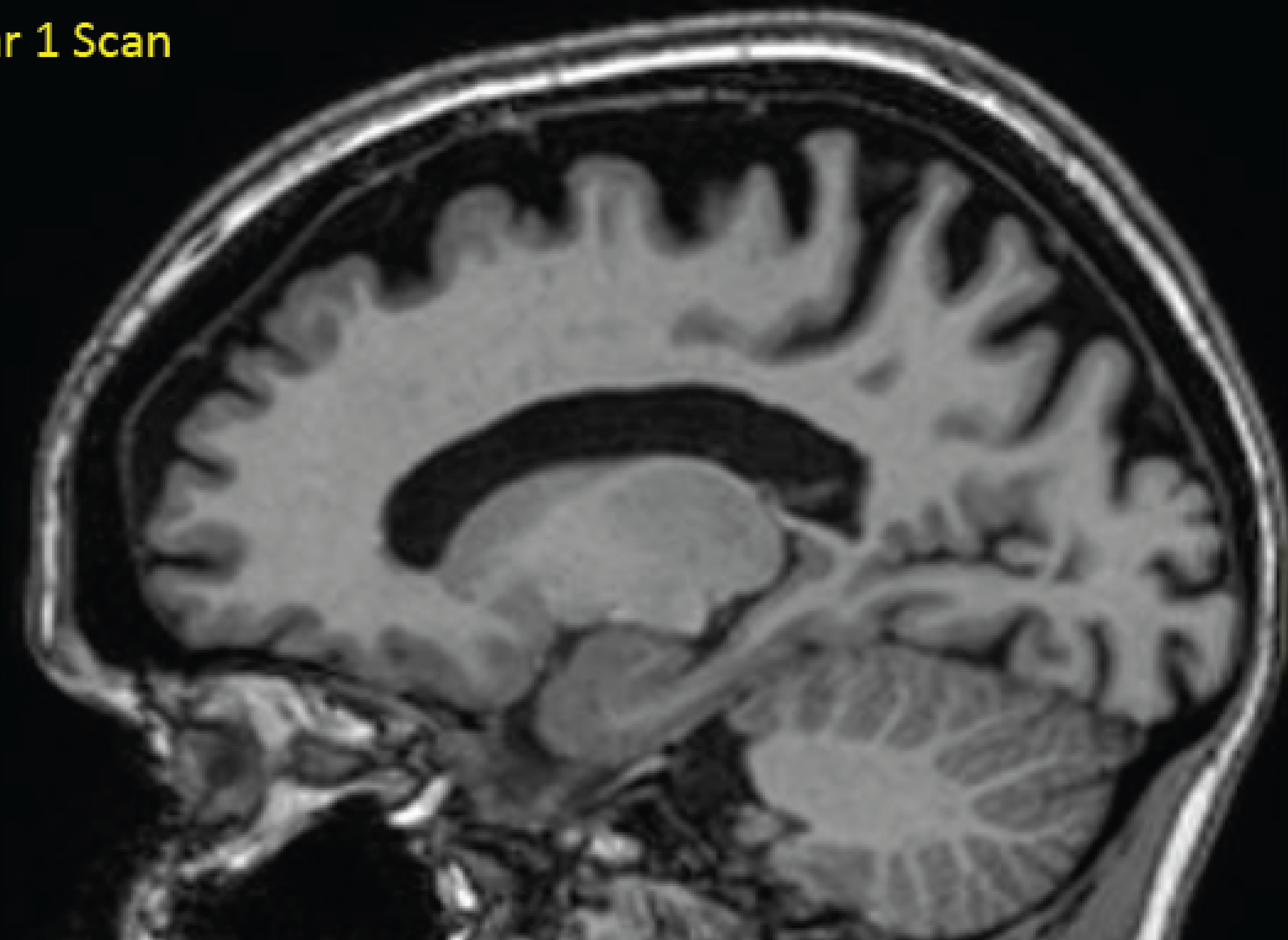
Baseline Scan



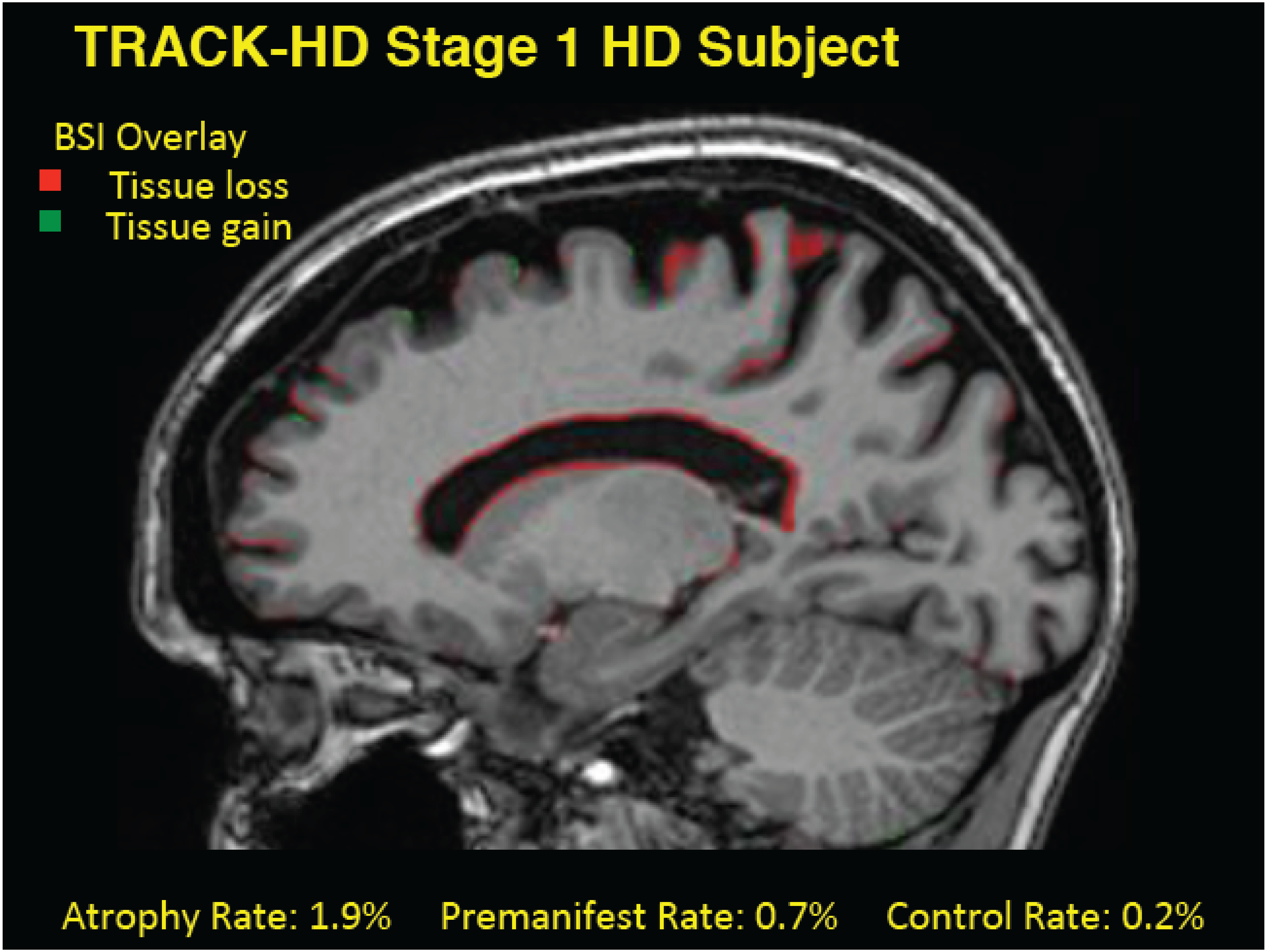
Courtesy Hans Johnsen, Jane Paulsen, IOWA

TRACK-HD Stage 1 HD Subject

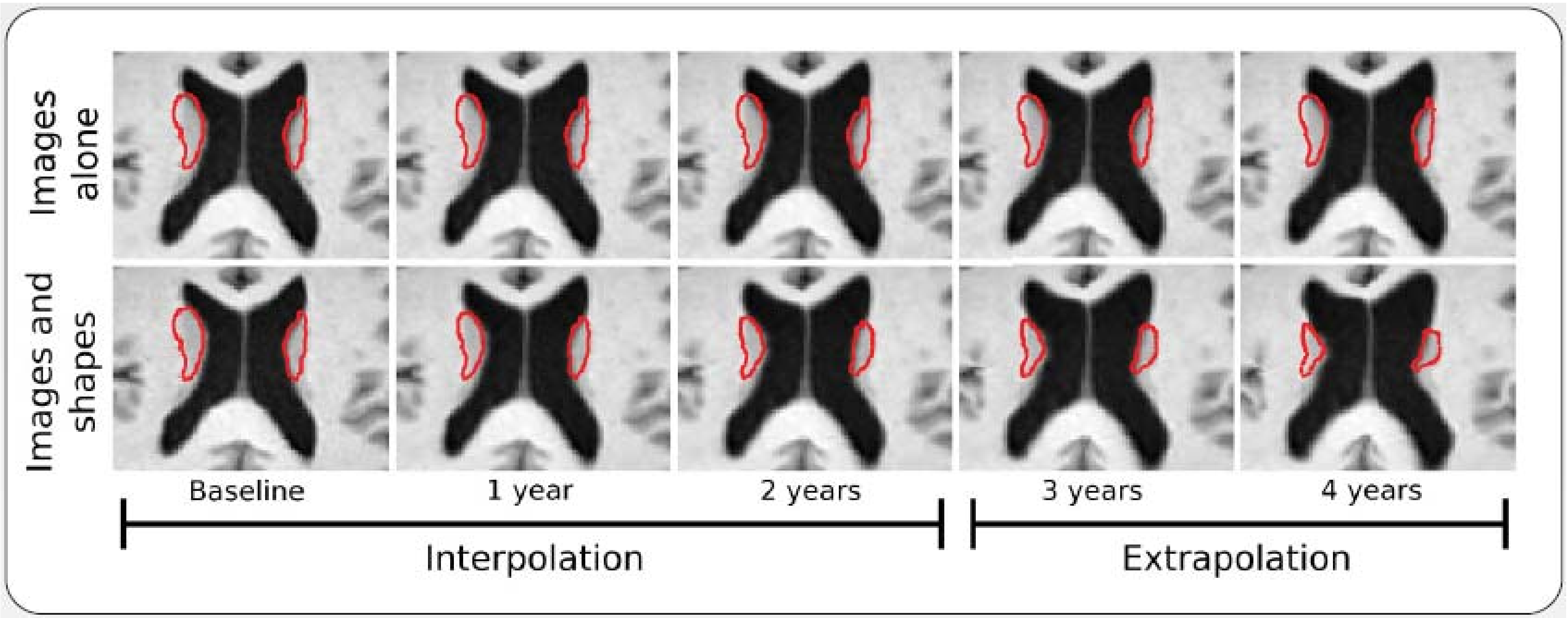
Year 1 Scan



Courtesy Hans Johnsen, Jane Paulsen, IOWA


TRACK-HD Stage 1 HD Subject
BSI Overlay
Tissue loss
Tissue gain
Atrophy Rate: 1.9%
Premanifest Rate: 0.7%
Control Rate: 0.2%

Huntington's Disease: Joint 4D Modeling of Shapes and Images

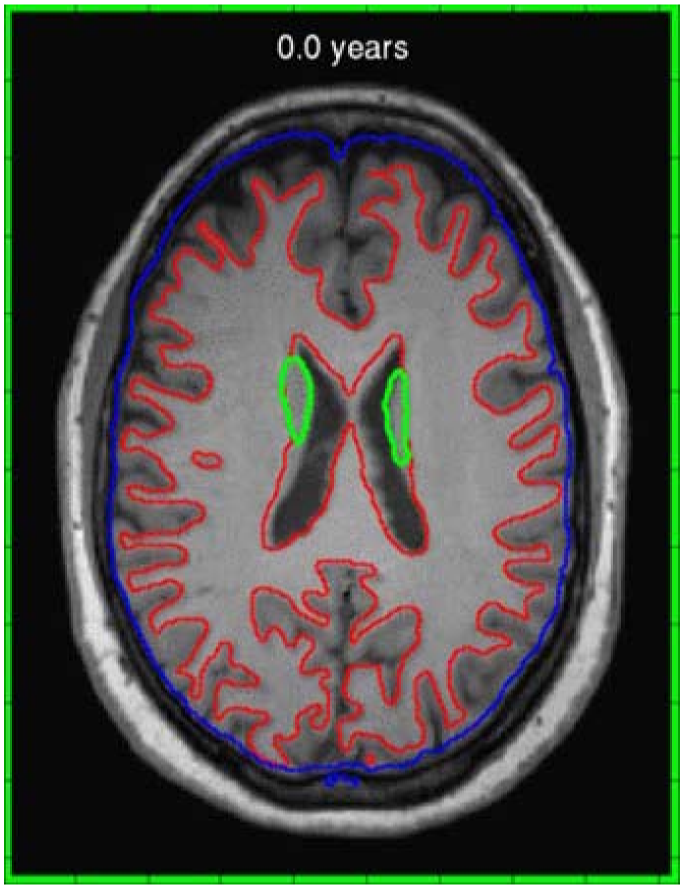


Single subject diagnosed with HD scanned at 58, 59, and 60 years of age.

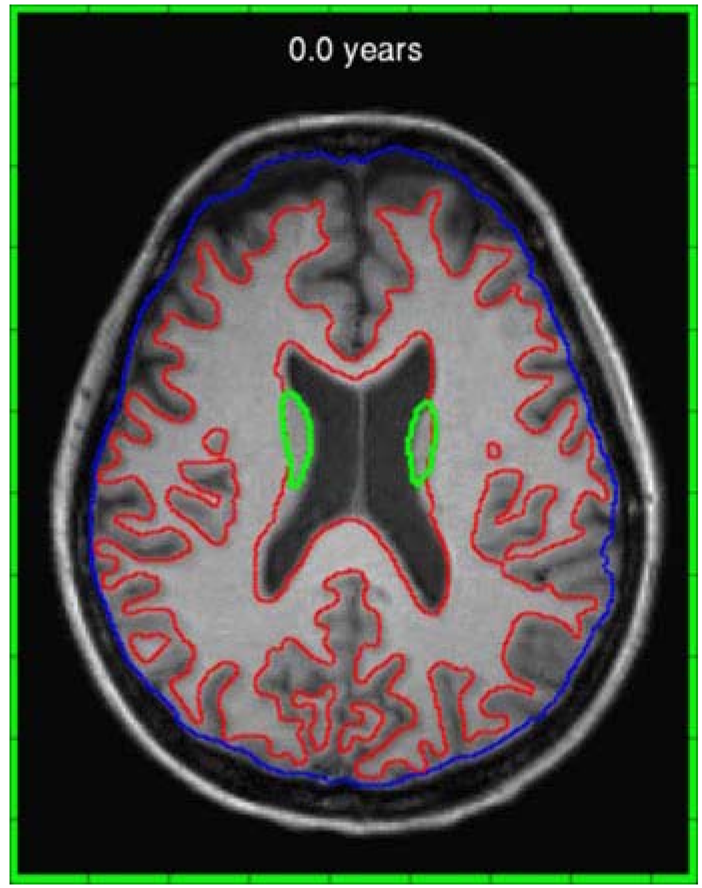
- T1W images.
- Left/right caudate segmented and manually cleaned.
- Geodesic model can be used to *extrapolate* into the future.

Subject-specific 4D shape & image regression

Control 2yrs Interval



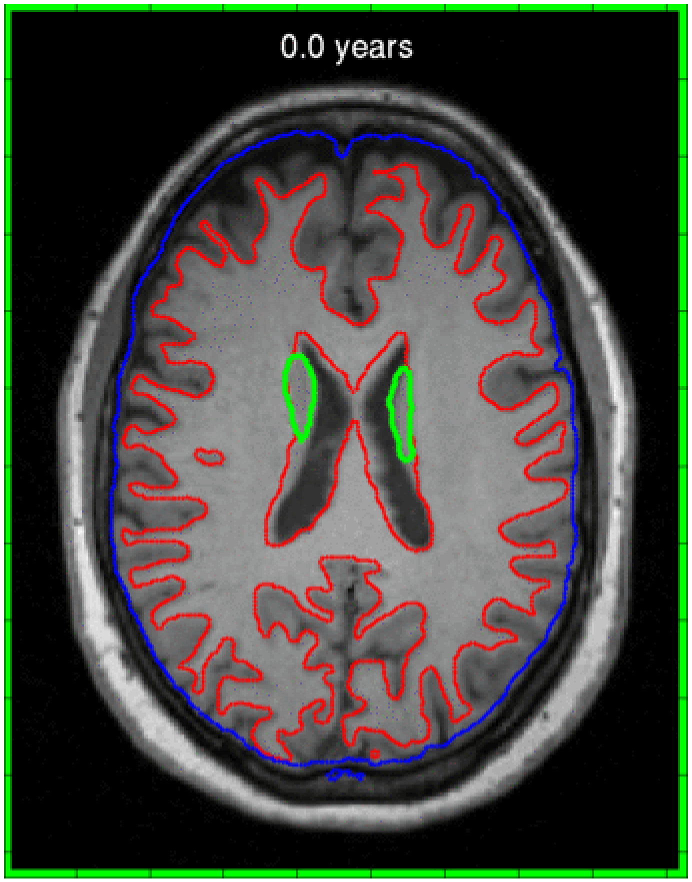
Huntington's D. 2yrs Interval



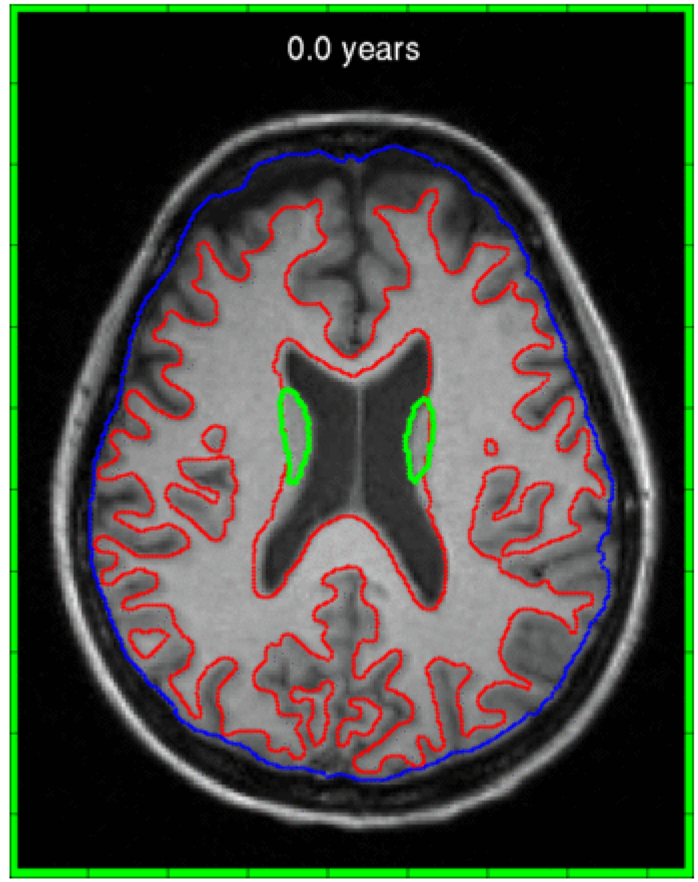
Fishbaugh et al., IPMI 2013

Work in Progress: Patient-specific 4D shape & image regression

Control Extrapolated



HD Extrapolated



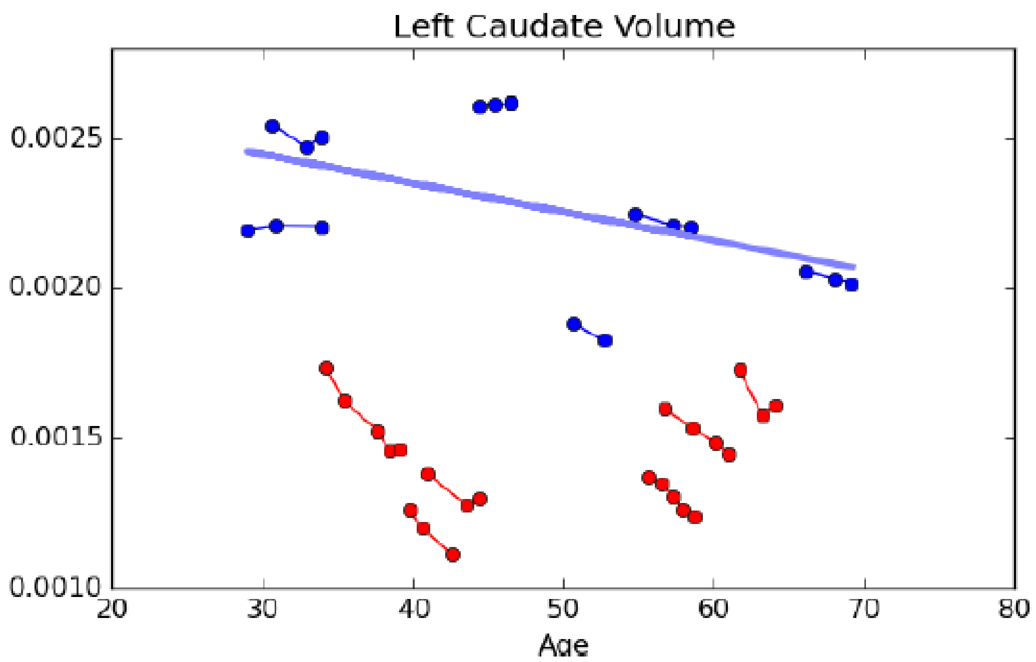
interpolation

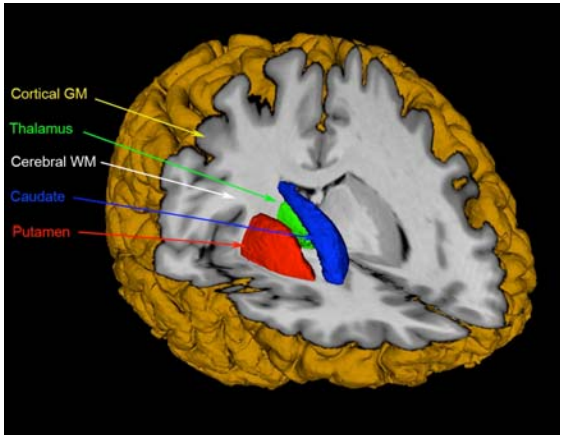
extrapolation

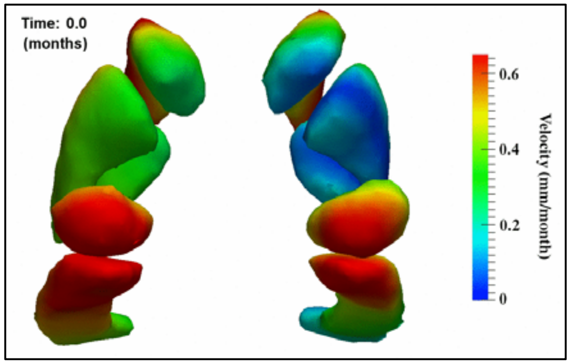
time

Fishbaugh et al., ISBI ‘13, IPMI ‘13

Huntington's Disease: Subject-specific models







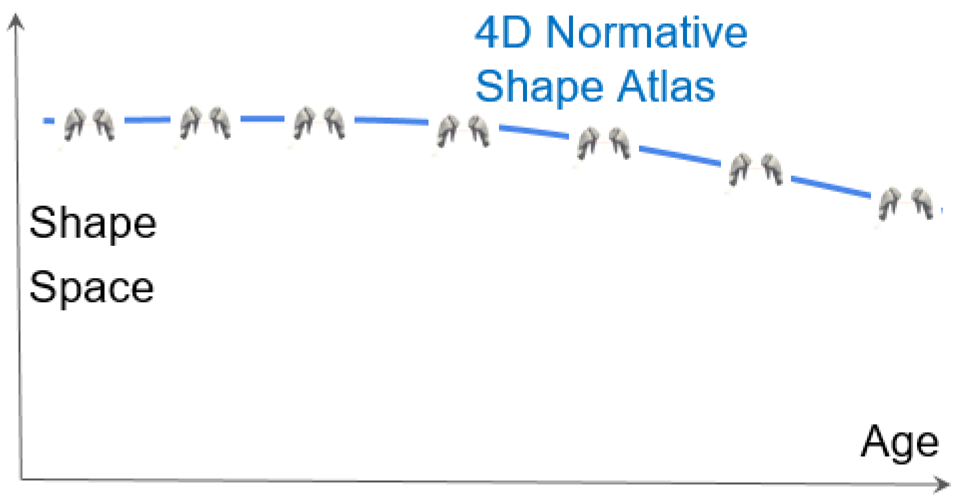
Caudate volume observations:

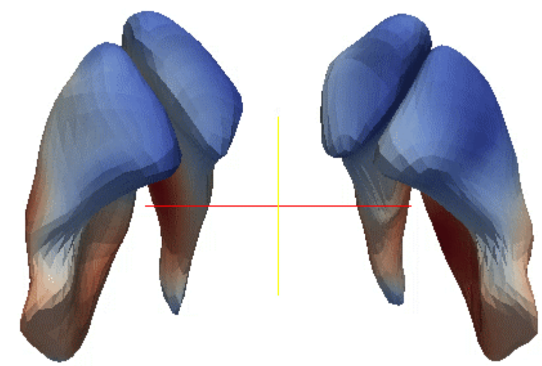
- control group (blue) and linear regression
- high risk group (red)

Collaboration Predict-HD, U-Iowa

Towards subject-specific analysis

4D Normative Atlas: Cross-sectional shape regression of controls

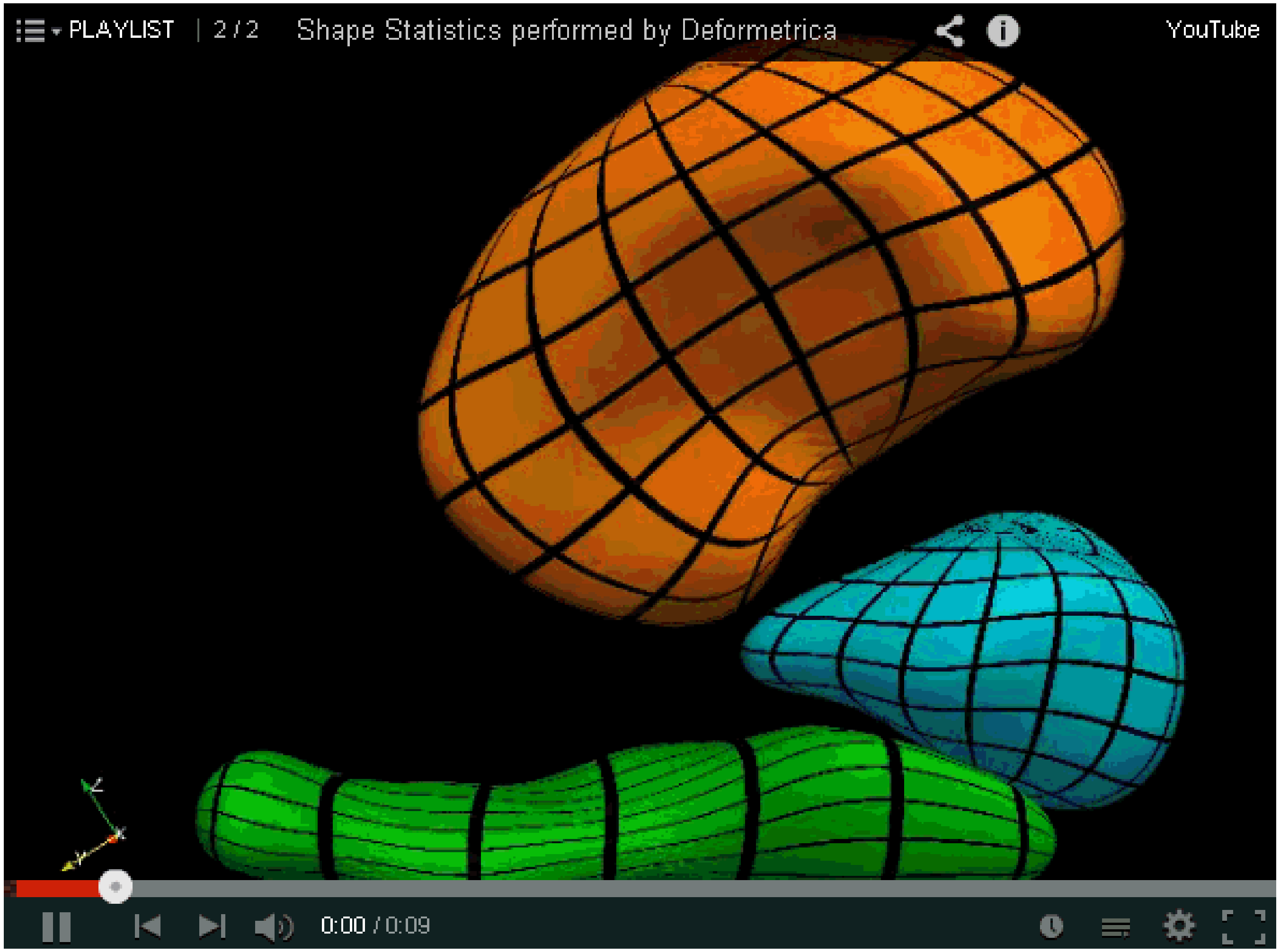




4D Normative Shape Atlas:
23 to 88 years, 243 subjects
Cross-sectional Regression

S. Hong et al, SPIE 2017

Statistics on Deformations

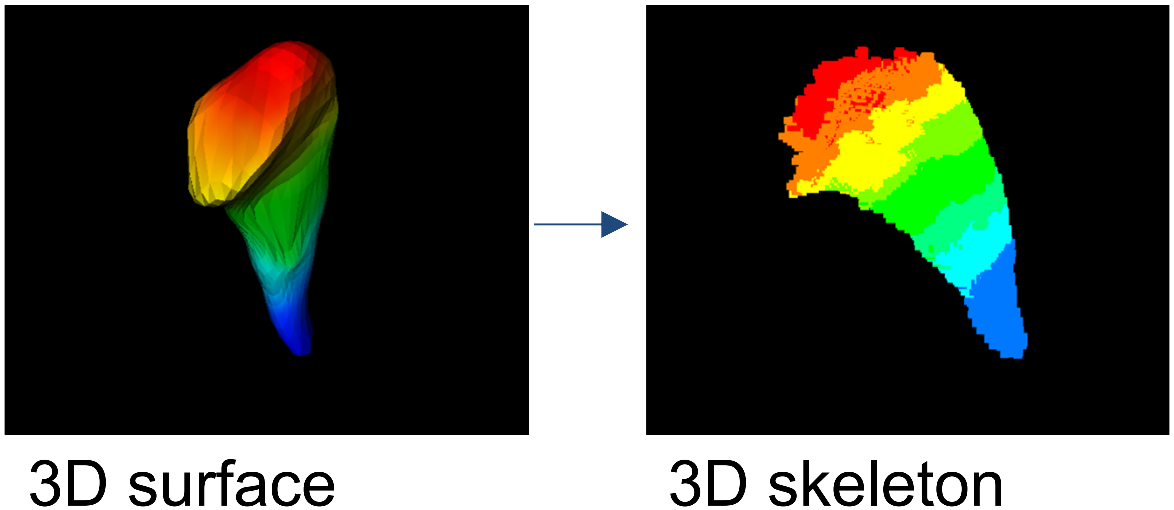


Most discriminative deformation axis between groups.

Durrleman et al, Neuroimage 2014

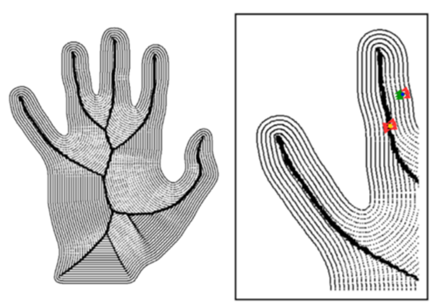
Towards subject-specific analysis

Shape Representation via 3D Skeleton



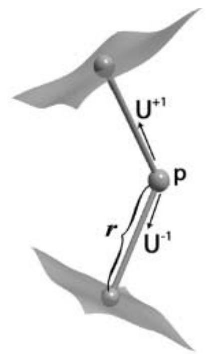
Color: corresponding points between surface and skeleton

- 3D skeletonization of shapes (Hamilton-Jacobian, Siddiqi et al.)
- Preliminary: Analysis of Thickness (Radii)



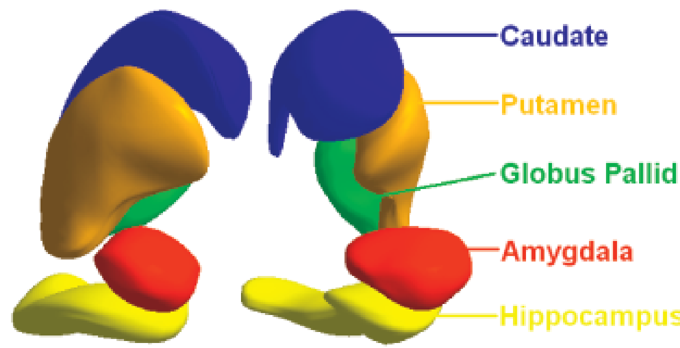
S. Hong et al, SPIE 2017

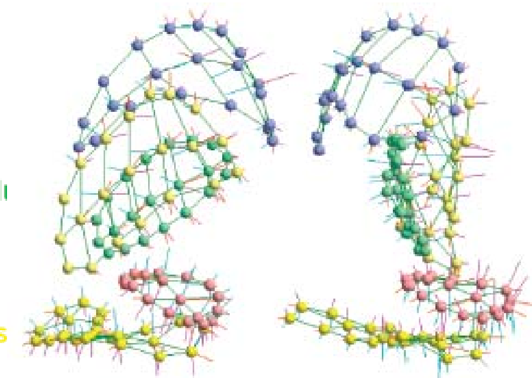
Medial Axis / Skeletal Representations: Intrinsic Shape Model



Medial atom: position (p), radius (r), and two normals to y (U).

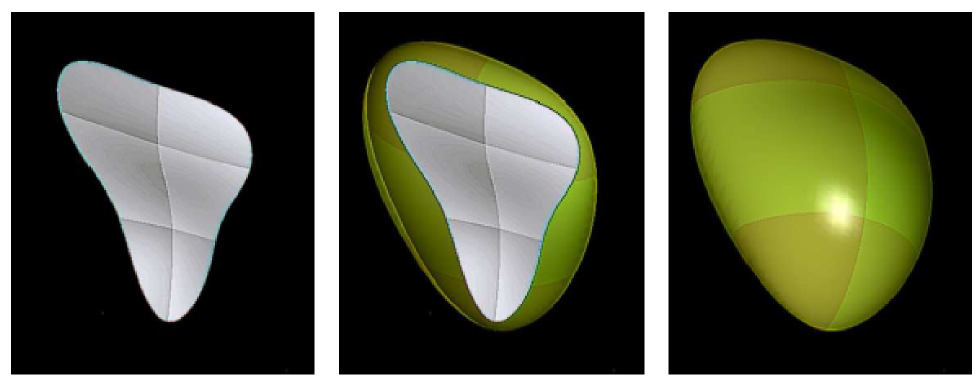
M-rep: Pizer et al.
(discrete)



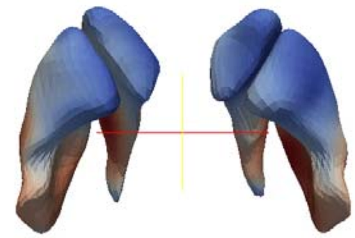


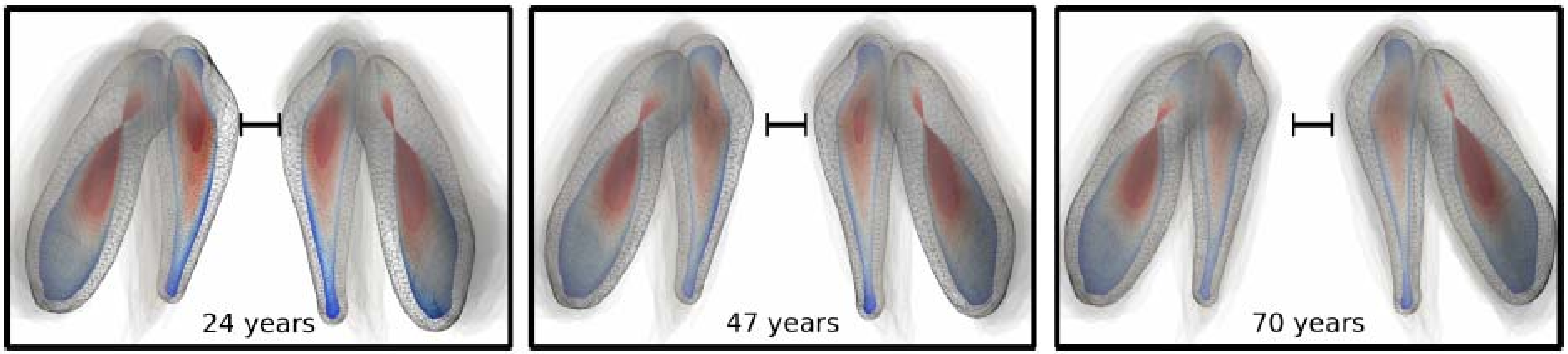
Gorczowski et al., T-PAMI 2010,
Stats on deformations vs. thickness

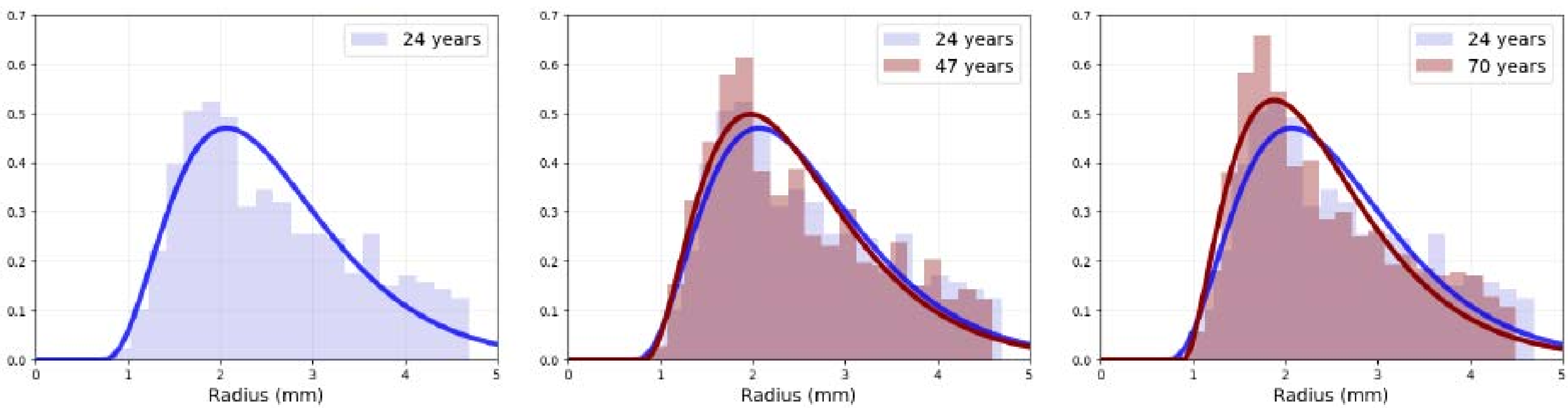
CM-rep: Yushkevich
(continuous, parametric)



Age-related changes: Pose & Shape



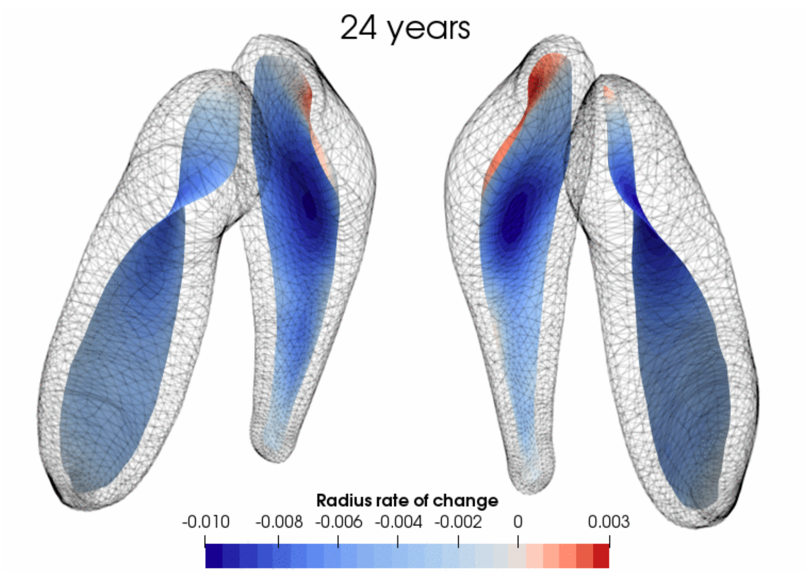


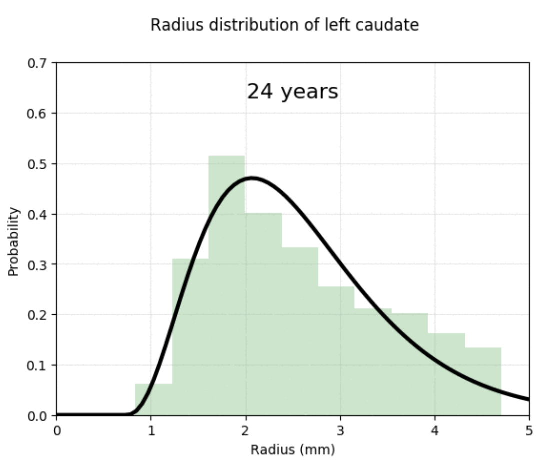


Skeletal radius histogram: Thinning from 24 to 70 years

S. Hong et al, submitted ISBI 2017

Preliminary Results





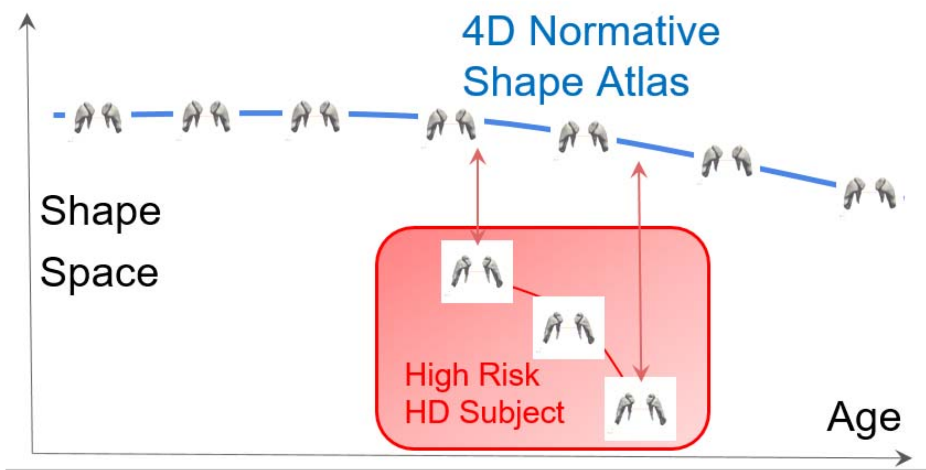
Shape Thinning/ Degeneration:

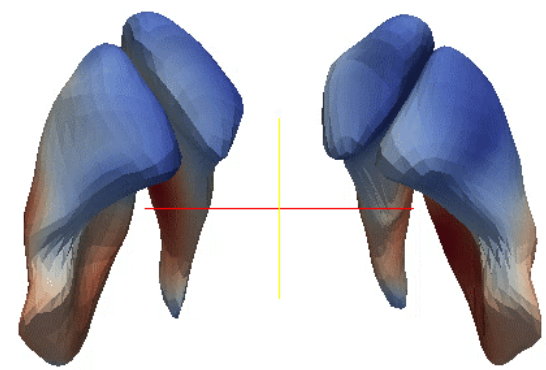
Shift to lower values (left)

S. Hong et al, submitted ISBI 2017

Towards subject-specific analysis

Question: Longitudinal Change in Normal versus Abnormal?



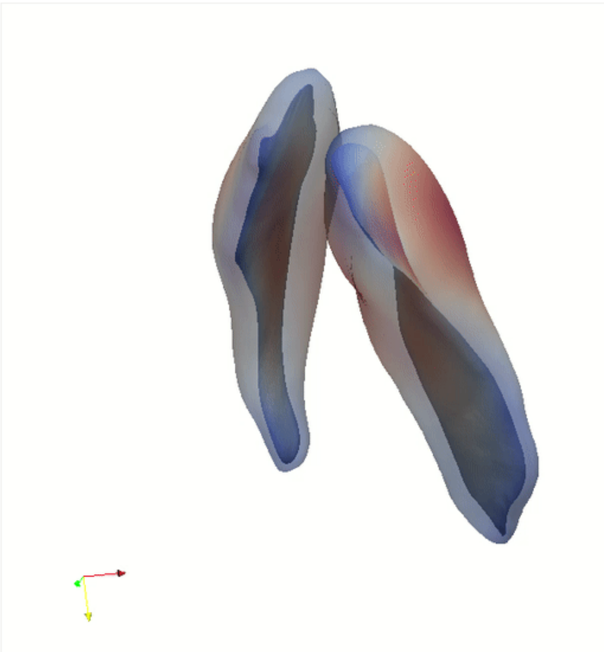


4D Normative Shape Atlas:
23 to 88 years, 243 subjects

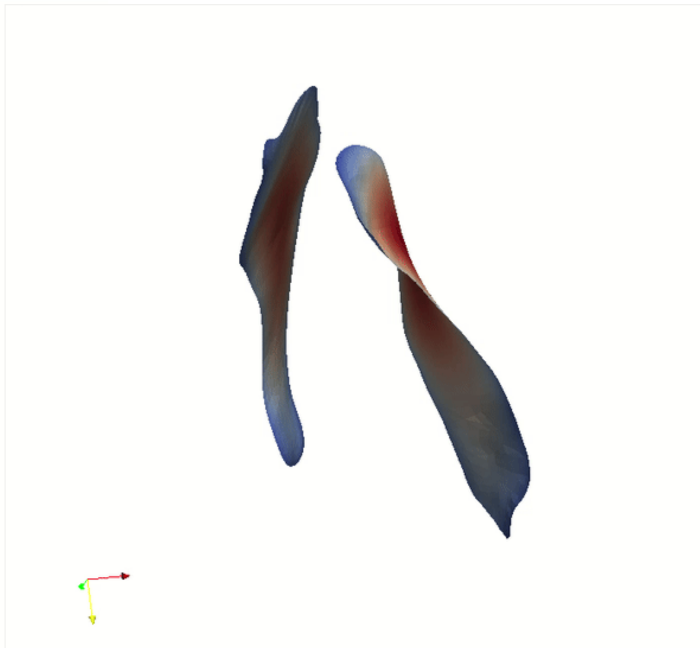
- Map 4D Model of Individuals into 4D Normative Atlas
- Analysis of Shape Distance to Norm: Decoupling of age versus pathological effects

S. Hong et al, SPIE 2017

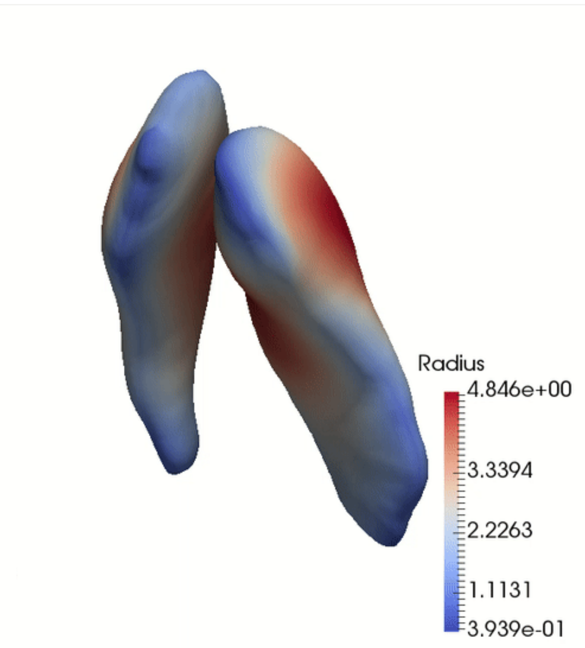
Multi-object example: Caudate Shape Trajectory



Caudate-putamen
Shapes with skeletons

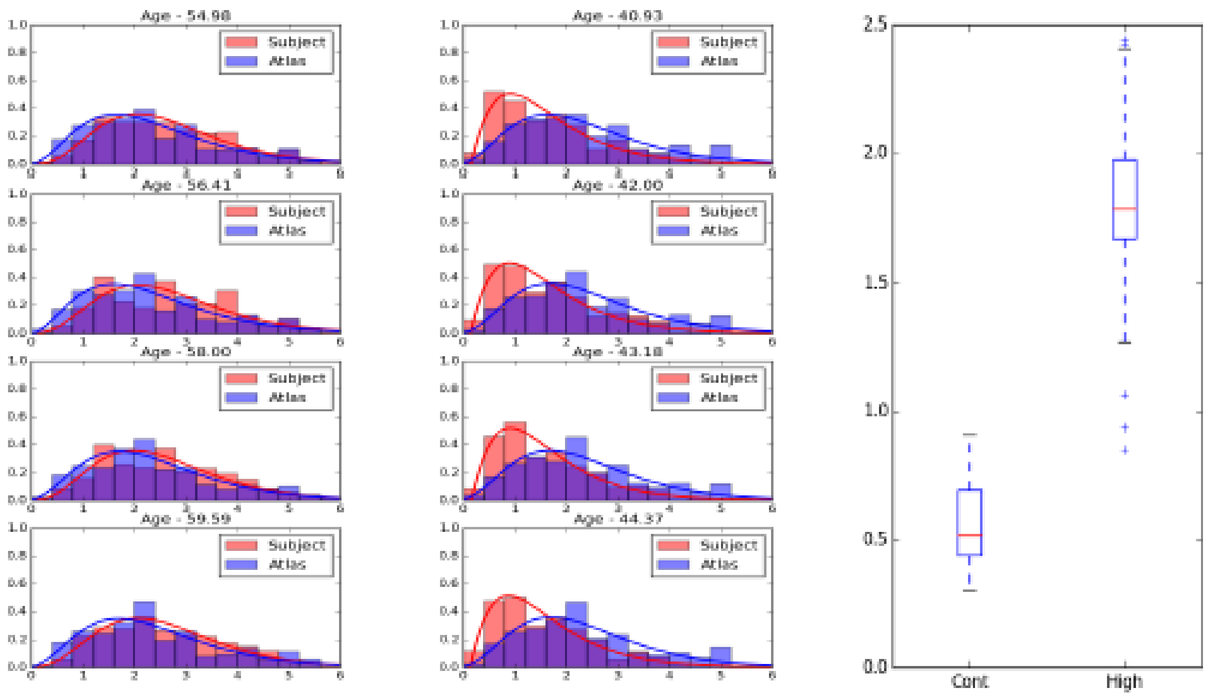


Skeletal representations



Reconstructions from skeletal intrinsic descriptions illustrating local radii/width information

Towards subject-specific analysis

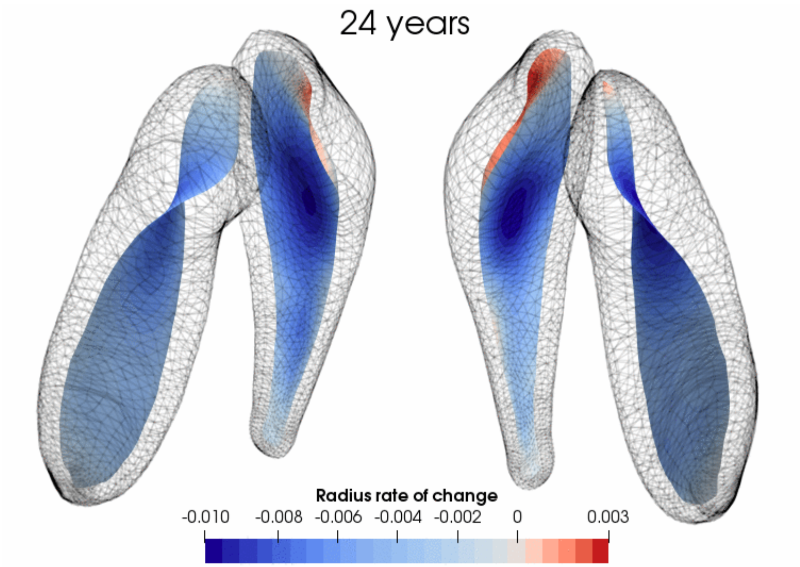


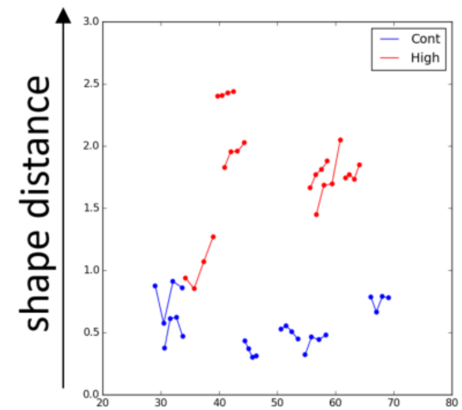
(a) Control (b) High (c) EMD box plot

- Comparison of individual's time points (red) to atlas (blue), age progression top to bottom.
- Quantitative analysis: Earth movers distance (EMD)

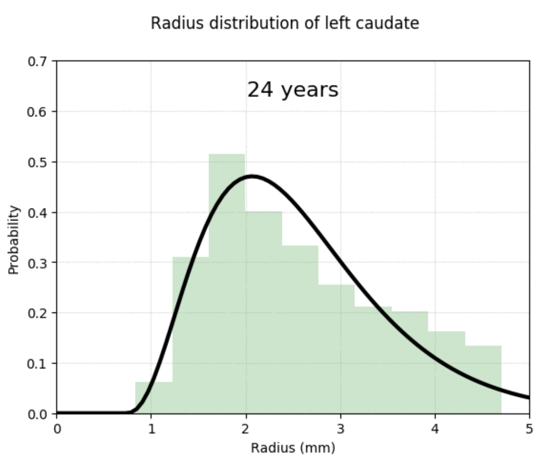
S. Hong et al, SPIE 2017

Preliminary Results





- Controls
- High Risk



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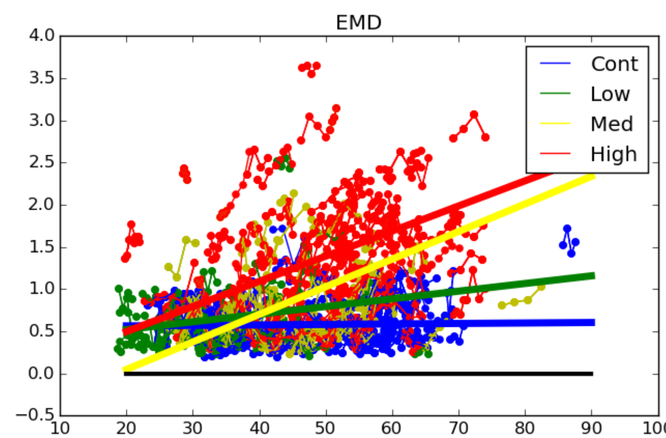


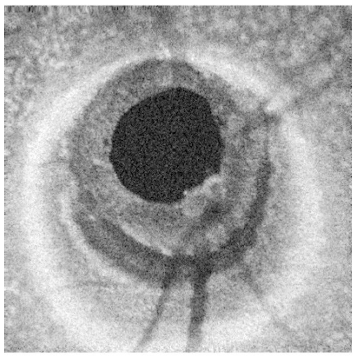
Presented Oct. 15 at NIH Conference

Contents

Glaucoma Research

H. Ishikawa, J. Schuman, Ch. Girot, J. Fishbaugh, G. Gerig

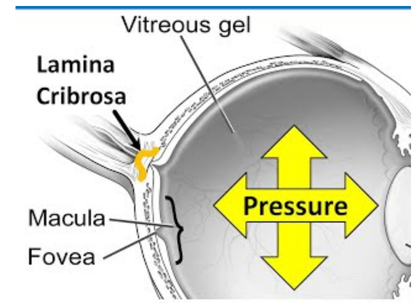
NYU Ophthalmology / Tandon

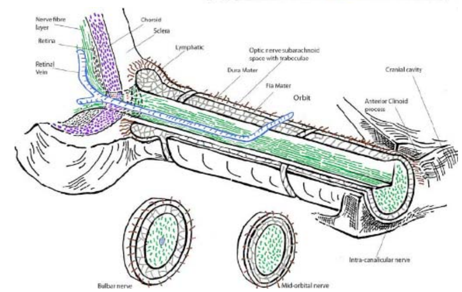


3D OCT

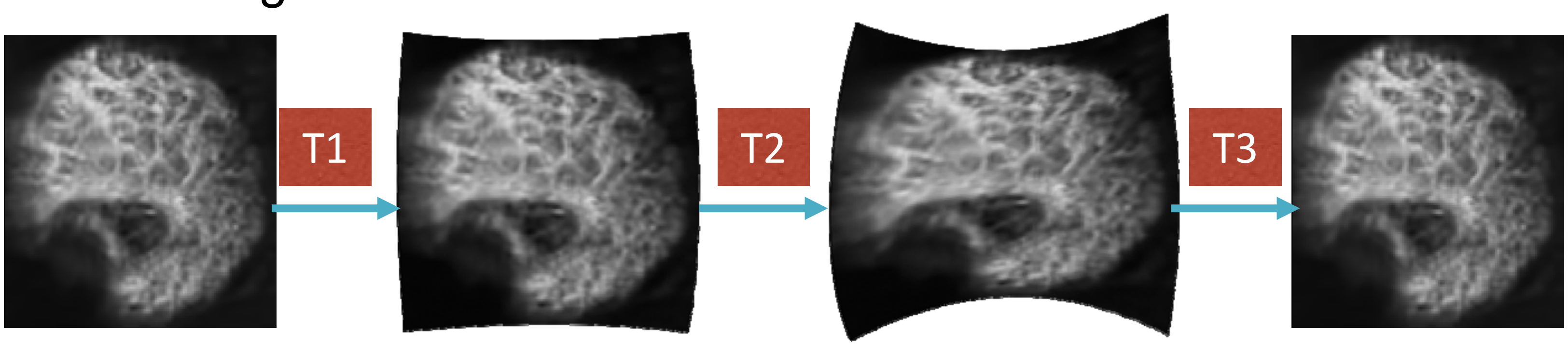
Goal:

- Pressure may cause axonal damage
- to study deformations of lamina cribrosa due to external pressure





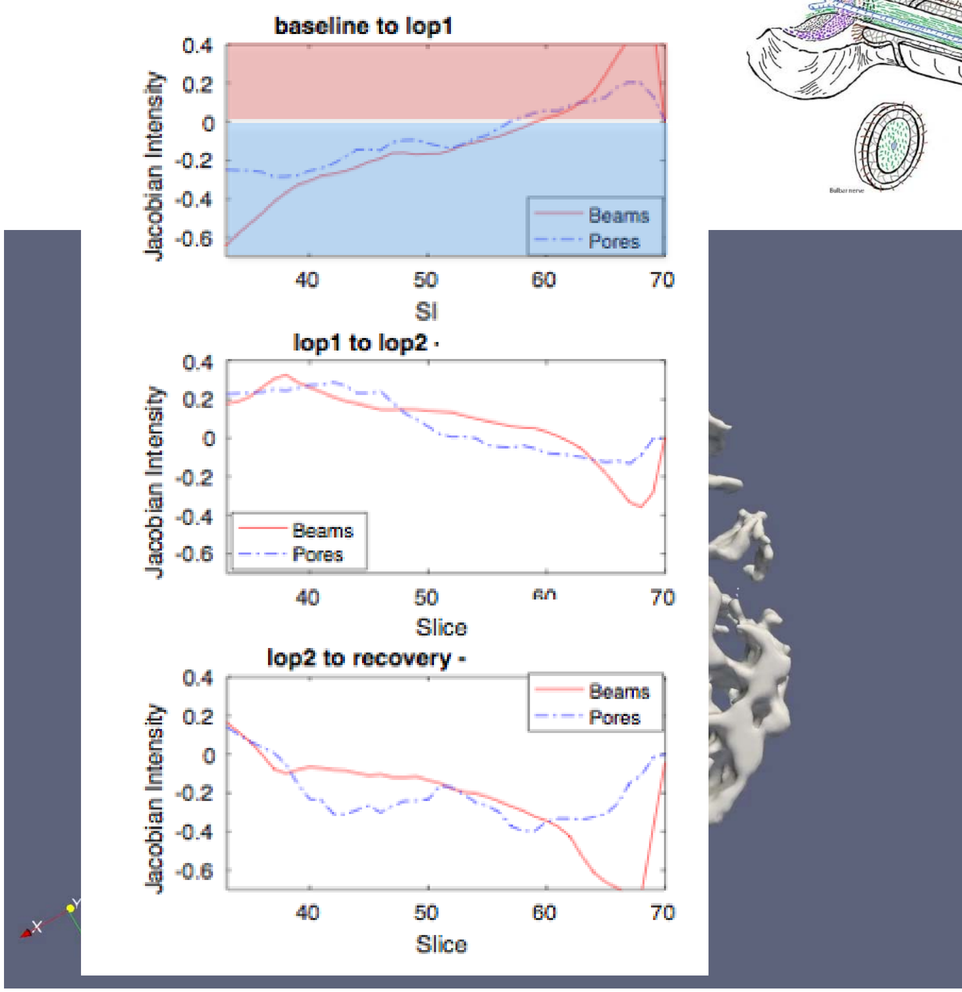
Clinical Design:

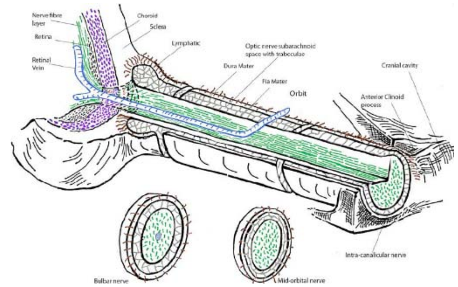


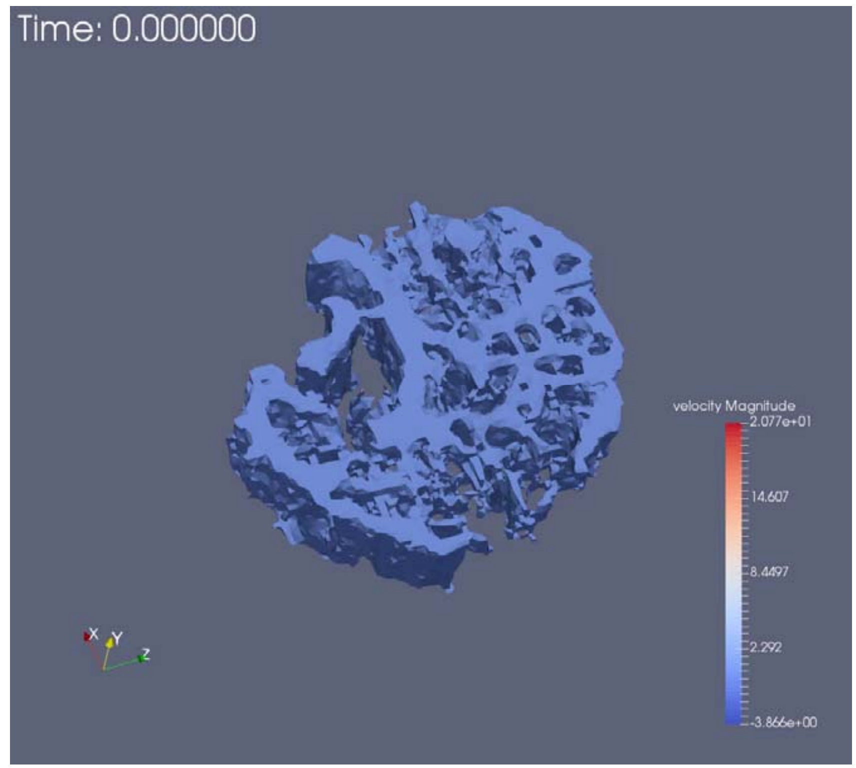
Baseline IOP1 IOP2 Recovery

Spatiotemporal Analysis of Lamina Cribrosa

Preliminary analysis of deformations



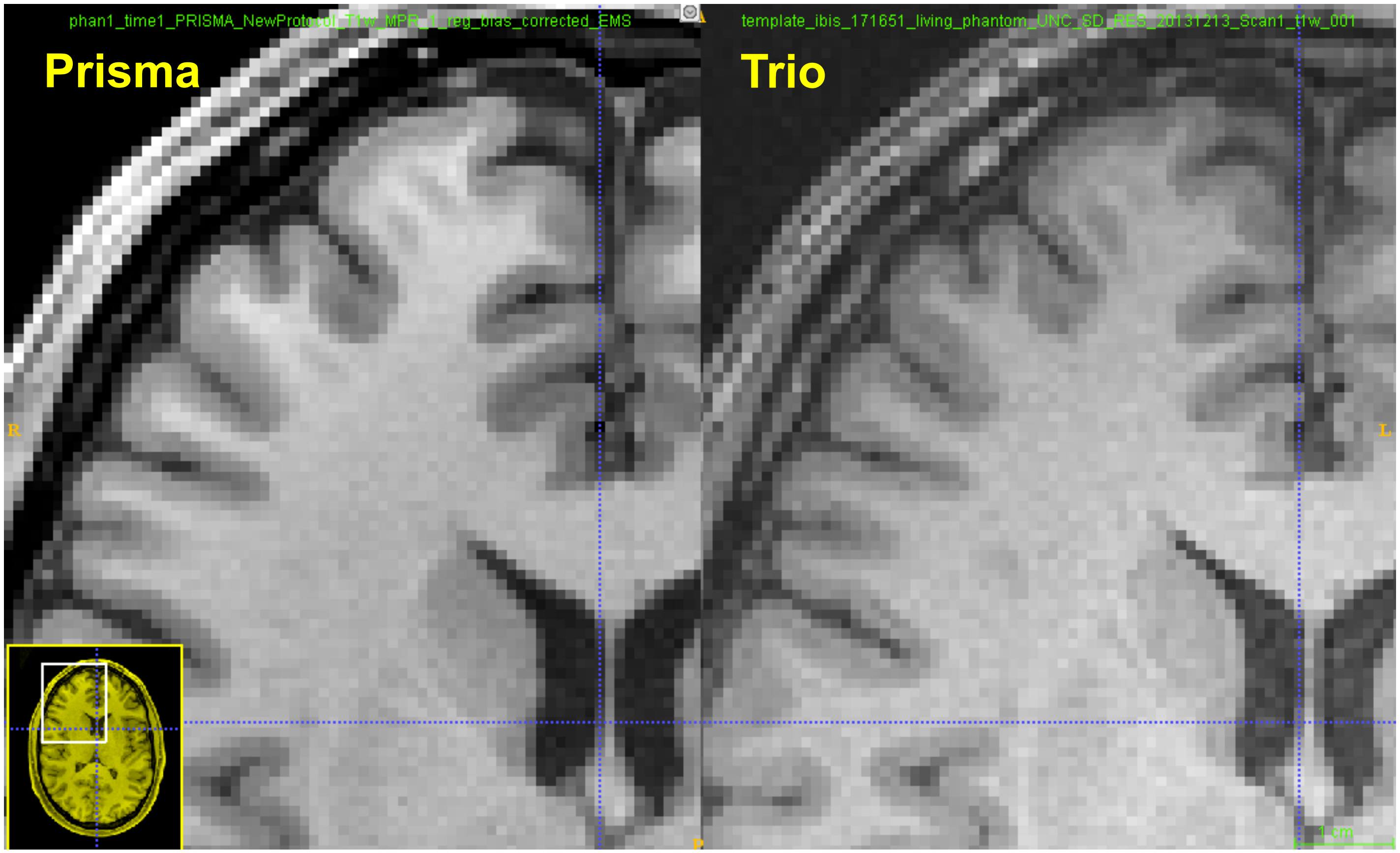




"Prisma Switch"

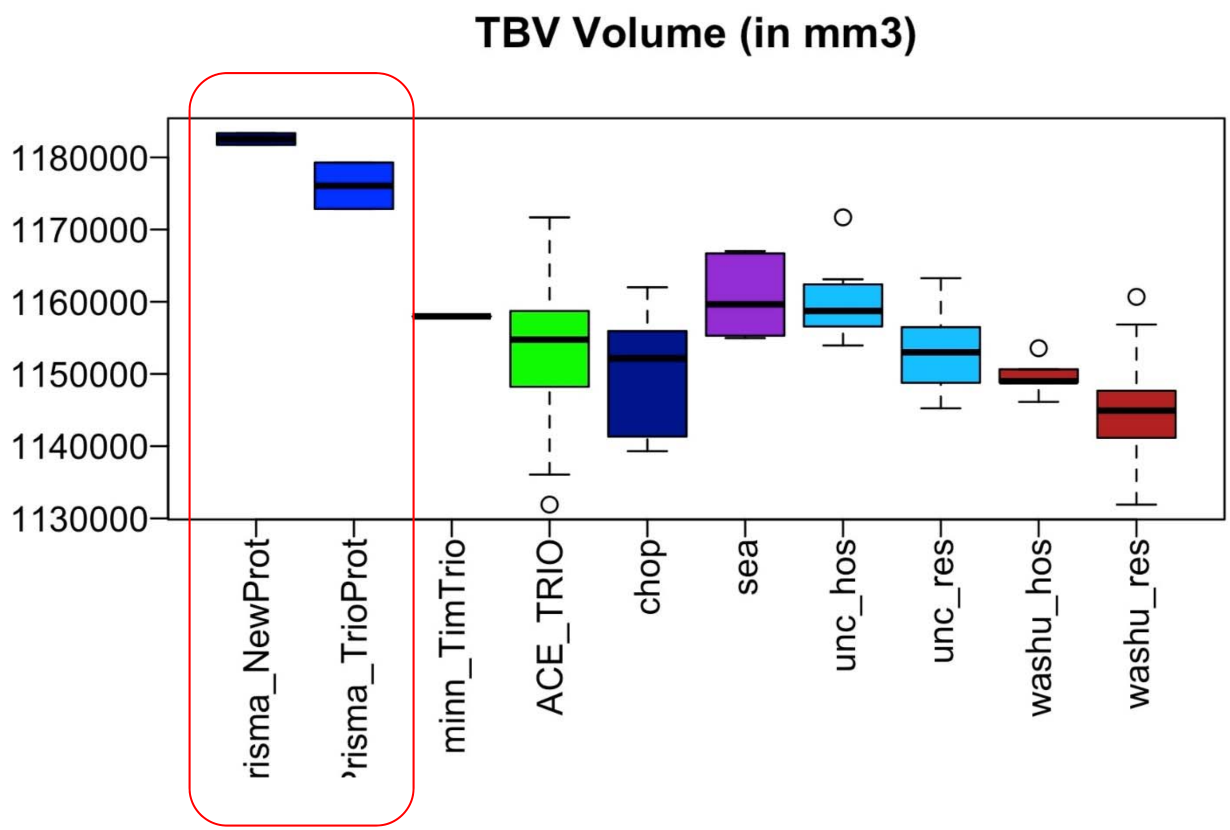
SIEMENS PR: The latest MRI technology will provide you with <u>virtually unlimited imaging and innovation capabilities</u> and long-lasting stability, even for long examinations – perfect for the most demanding research quests.

Good News: Prisma Images are beautiful!



MRI: Prisma versus Trio: Traveling Phantom SD

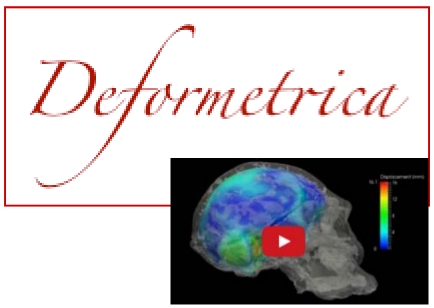
But: Established Processing provides differences for Prisma

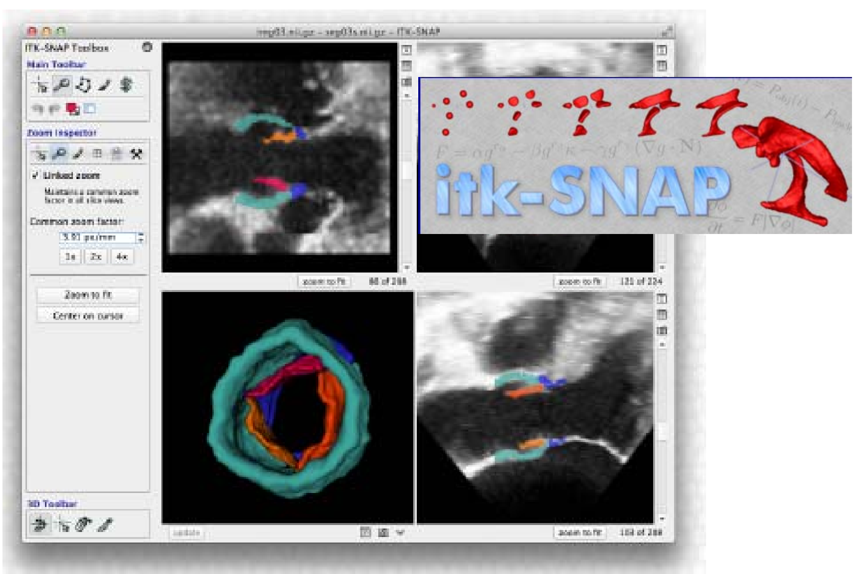


Human traveling phantoms, repeated annual scans over 3 years

Software Engineering & Sharing

- Open-source/open-platform
- Industrial collaborations





Conclusions

- Spatio-temporal 4D Image & Shape Analysis:
  - Most clinical neuroimaging studies include longitudinal design.
  - Challenging fundamental, algorithmic and statistical problems.
  - Research progress enables new scientific discoveries.
- Clinically relevant for quantitative analysis of <u>subject-specific, personalized changes</u> due to disease or therapy.
- Longitudinal data benefits from longitudinal image analysis ≠ cross-sectional analysis
- Image data (autism) freely available to public via NIH NDAR
- Challenges:
  - Image data calibration across scanners/time: DL promising
  - 4D data: Annotated data? High-dim data?

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NIH NIBIB 1R01EB014346-01: ITK-SNAP

NIH NINDS R01 HD067731-01A1: Down's Syndrome

NIH P01 DA022446-011: Neurobiological Consequences of Cocaine Use

- **Insight Toolkit ITK**

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