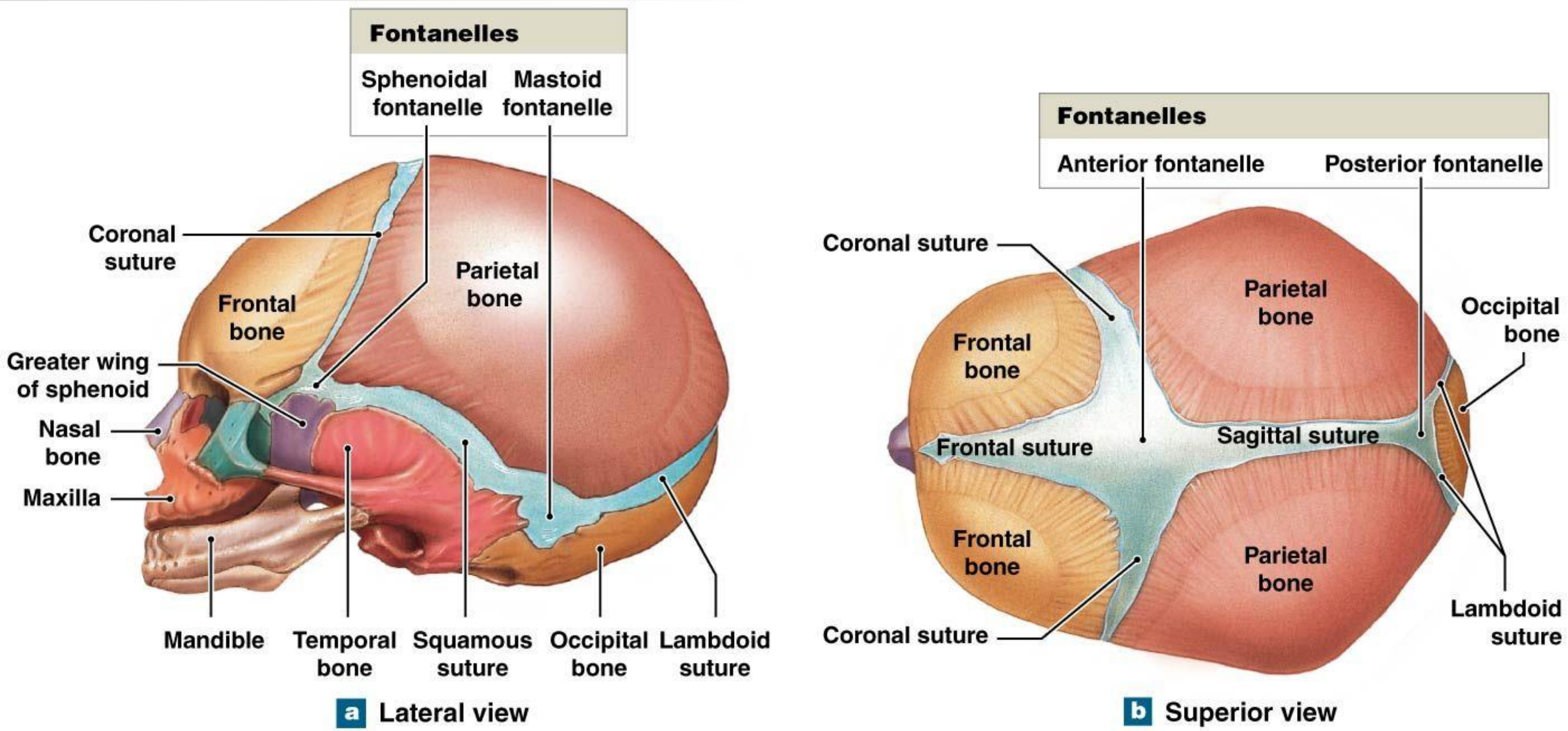
Statistical Shape Analysis of Infant Skull

Ezgi Mercan
Ezgi.Mercan@SeattleChildrens.org

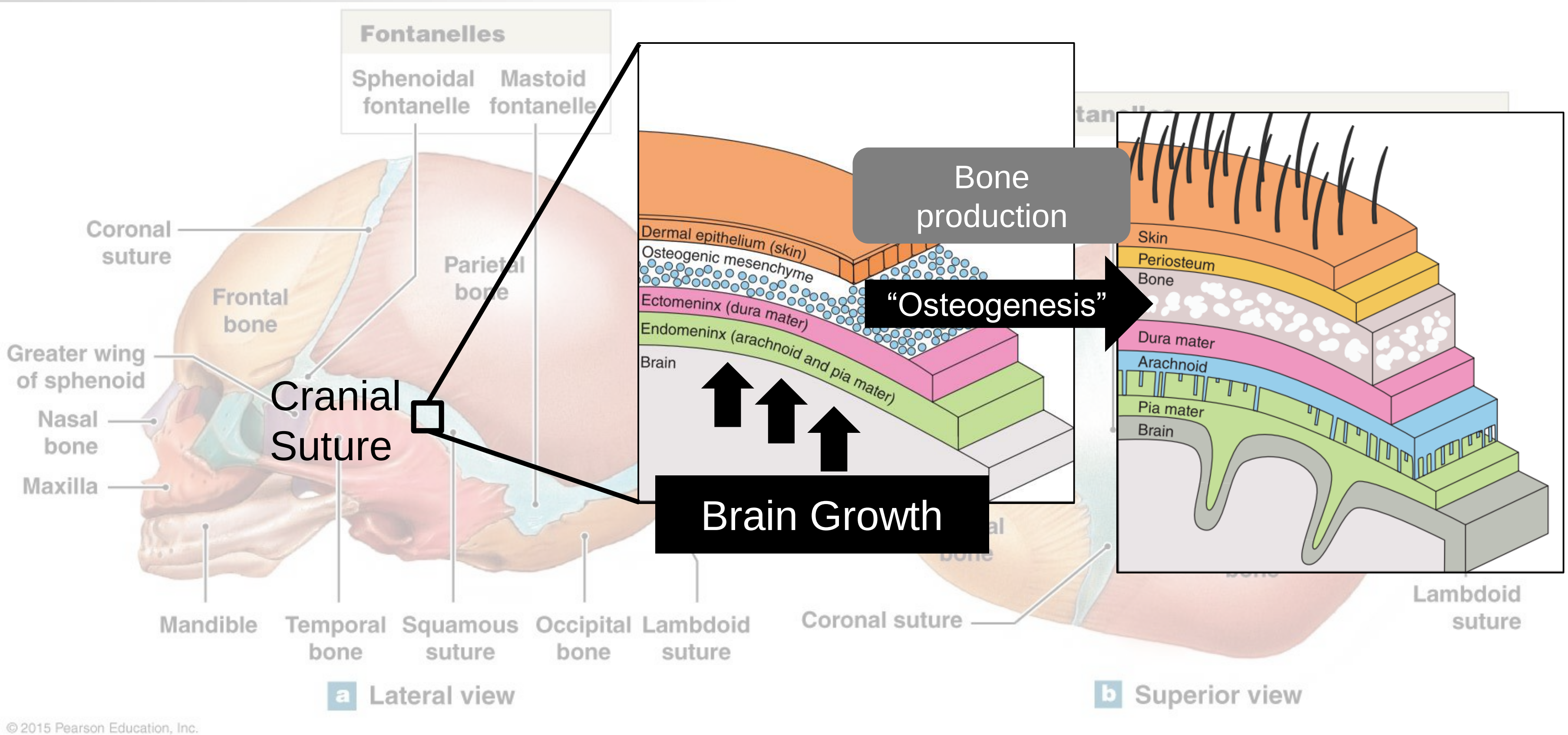
Infant Skull

- A newborn skull is 25% of its adult size and doubles in size by the first 6 months.



Infant Skull

- A newborn skull is 25% of its adult size and doubles in size by the first 6 months.
- Brain growth "drives" skull growth at 5 major cranial sutures.

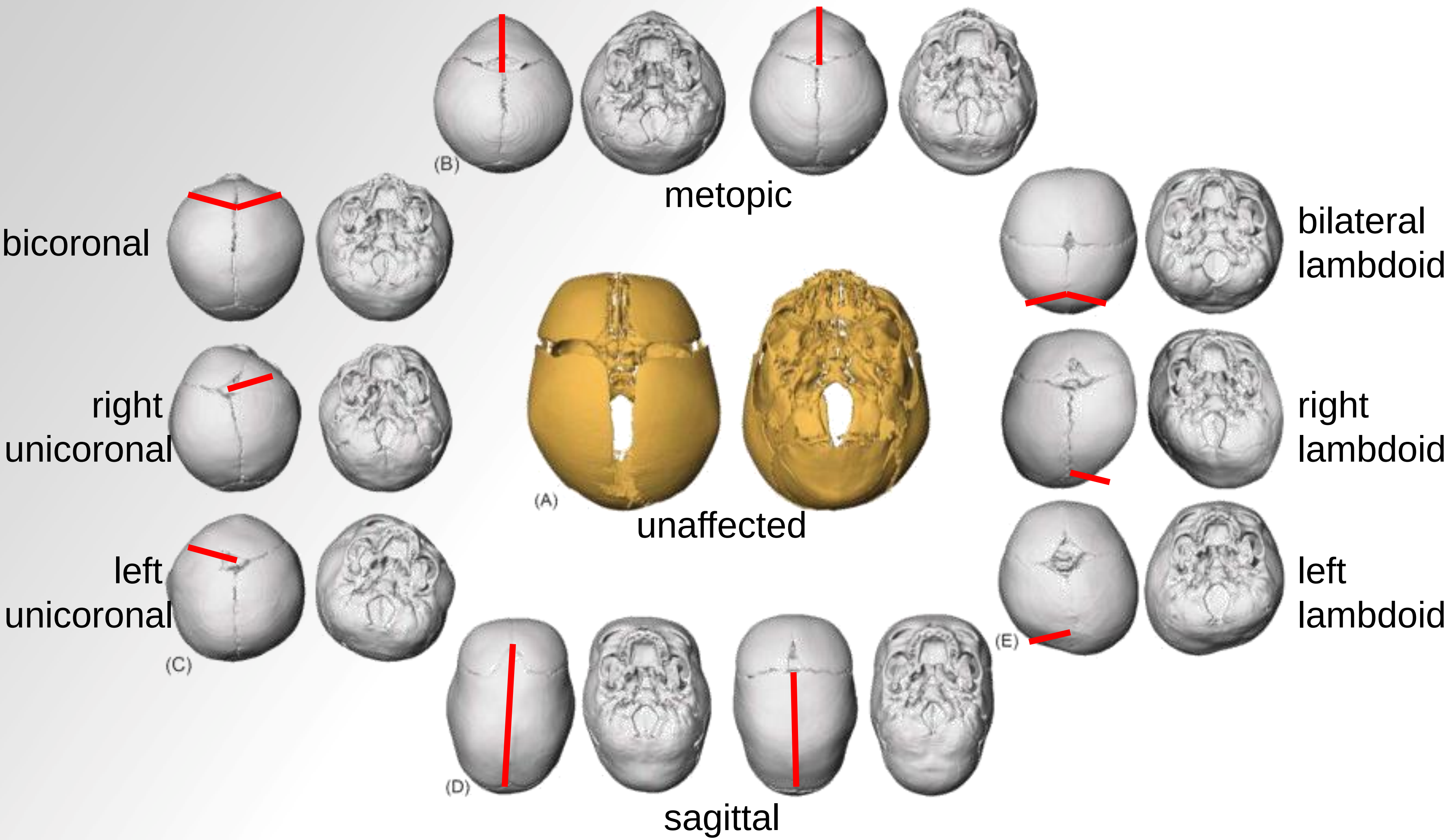


Flaherty K, Singh N, Richtsmeier JT. Understanding craniosynostosis as a growth disorder. *Wiley Interdiscip Rev Dev Biol*. 2016;5(4):429-459. doi:10.1002/wdev.227

Craniosynostosis

- A congenital disease involving premature fusion of cranial sutures.
- 1 in every 2000-2500 newborns has craniosynostosis.
- Infants present with "abnormal" head shape, ridge over the fused suture and smaller soft spot (fontanelle).
- Definitive diagnosis requires a CT scan.
- Each year we care for more than 400 children with craniosynostosis.
- Treatment involves plastic surgery: cranial reconstruction.
- If untreated, it may cause increased intracranial pressure and developmental delays.

Skull Shape in Craniosynostosis



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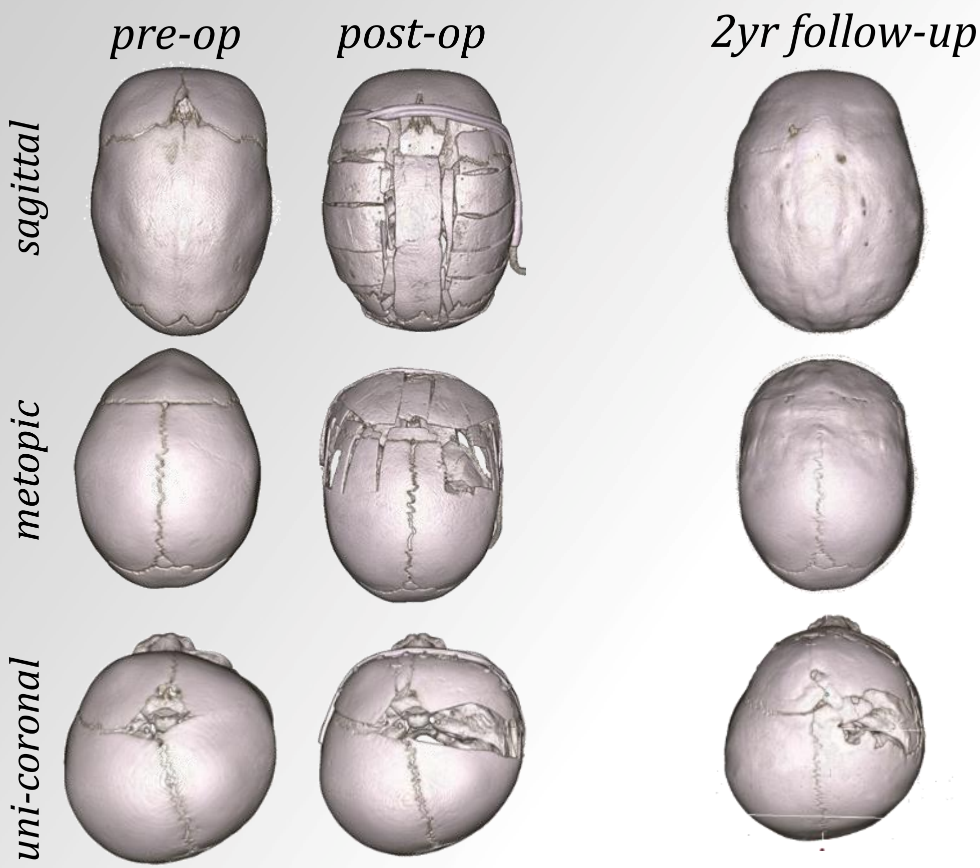
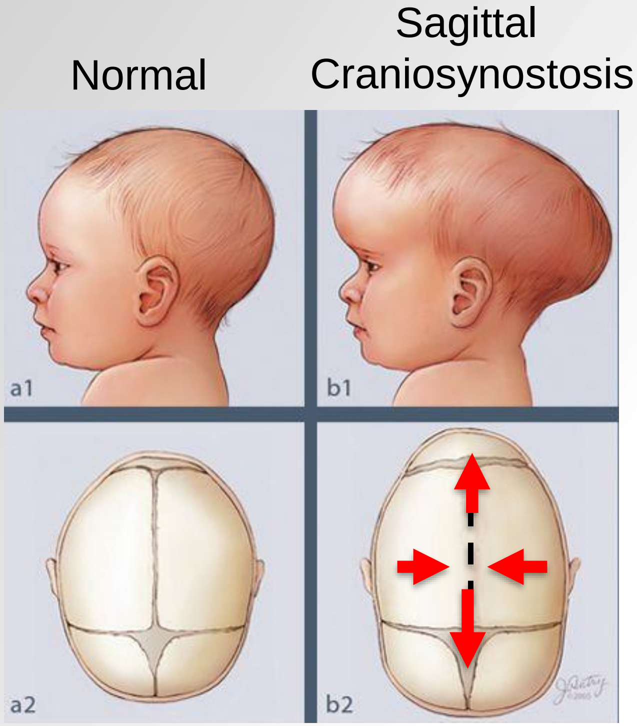
Cranial Reconstruction



- Shape maintenance
- What *changes* are due to growth ?
- What *factors* affect the long-term outcome?
    - Timing of the repair
    - Initial severity
    - Individual characteristics
- How does the skull *grow* in different diagnoses?

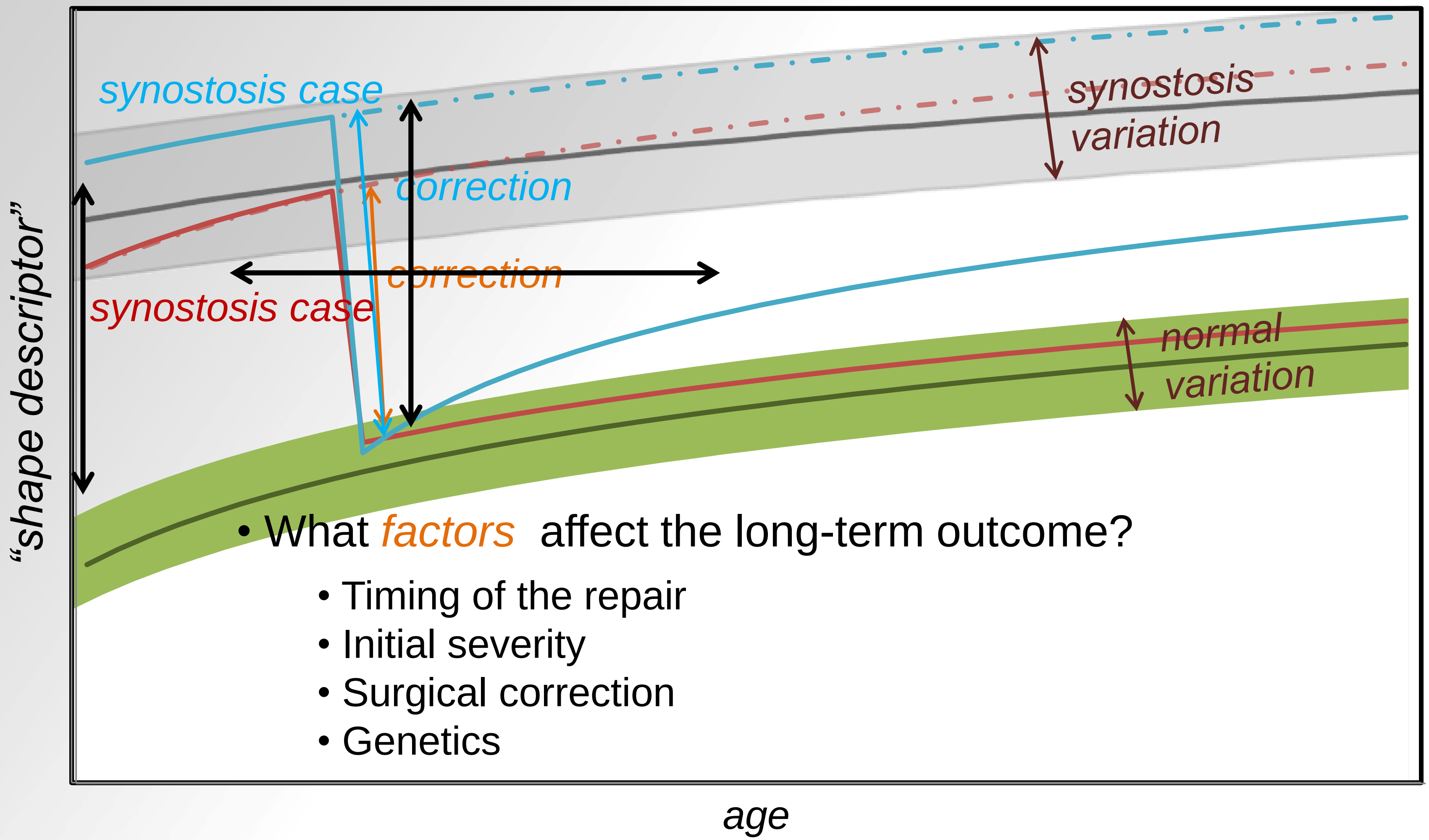
Goal: minimal surgical intervention

Current Theory of Growth in Synostosis



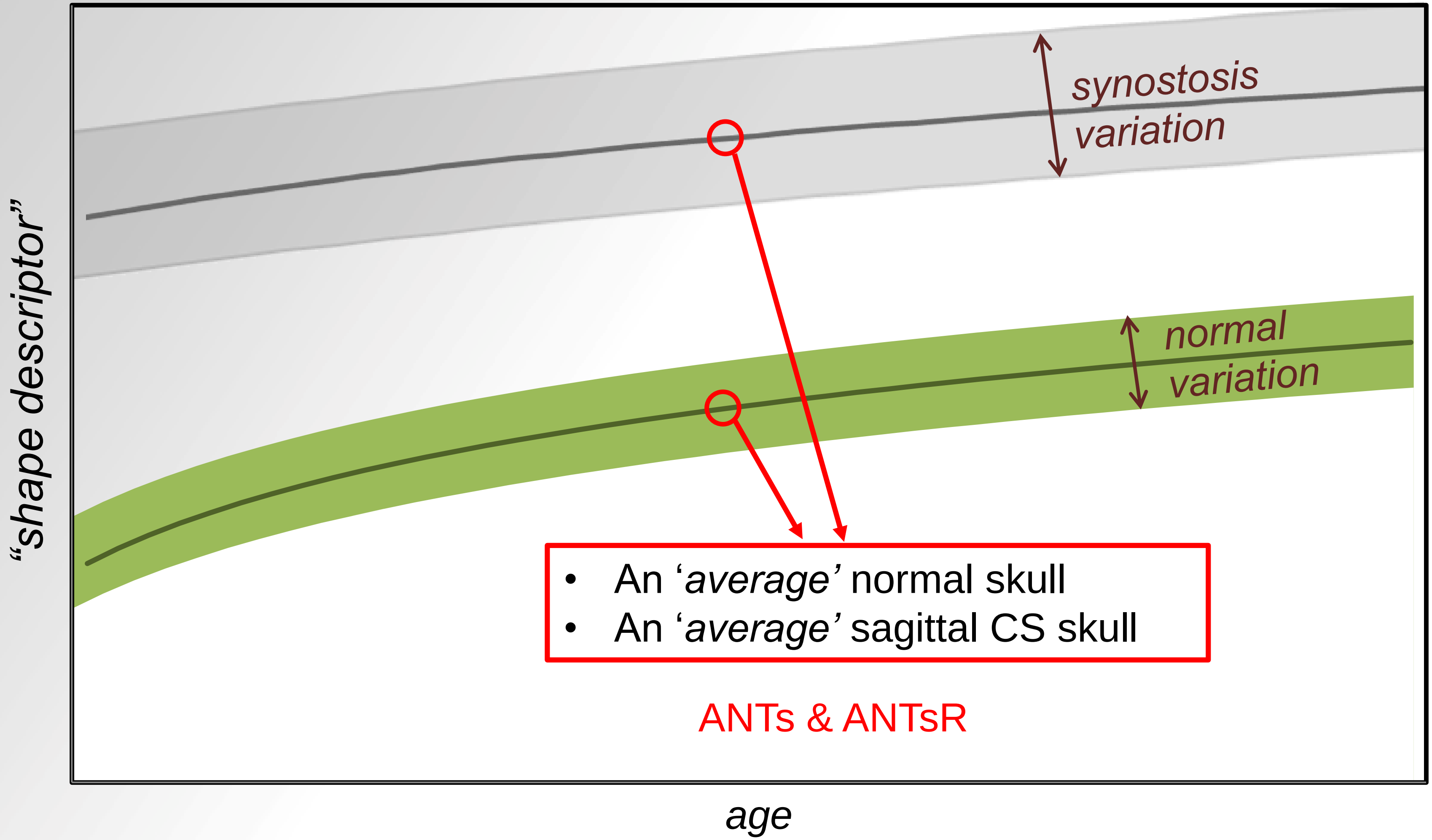
Virchow (1851): During craniosynostosis, skull growth
– is restricted to a plane perpendicular to the affected, prematurely fused suture and
– is enhanced in a plane parallel to it.

Hypothetical Growth



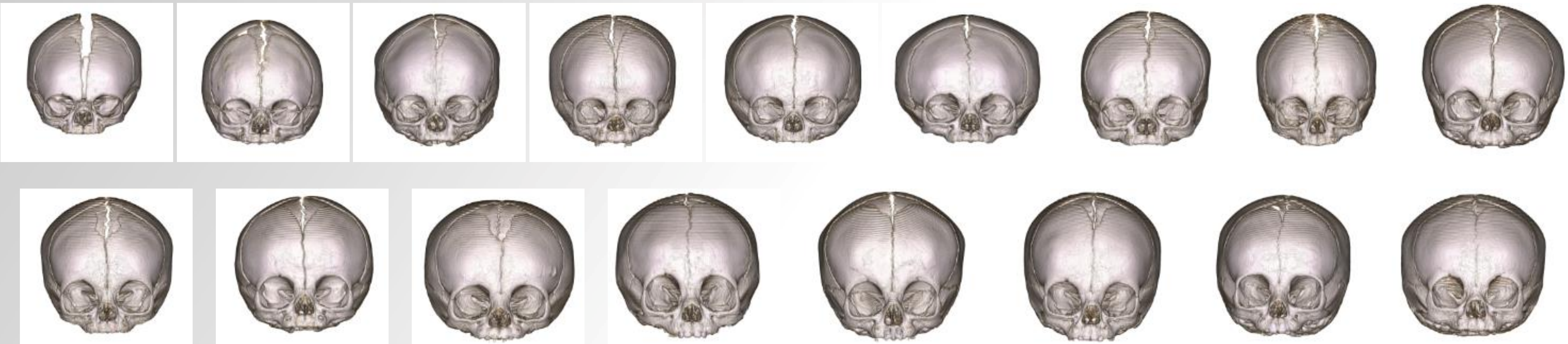
- What *factors* affect the long-term outcome?
  - Timing of the repair
  - Initial severity
  - Surgical correction
  - Genetics

Hypothetical Growth

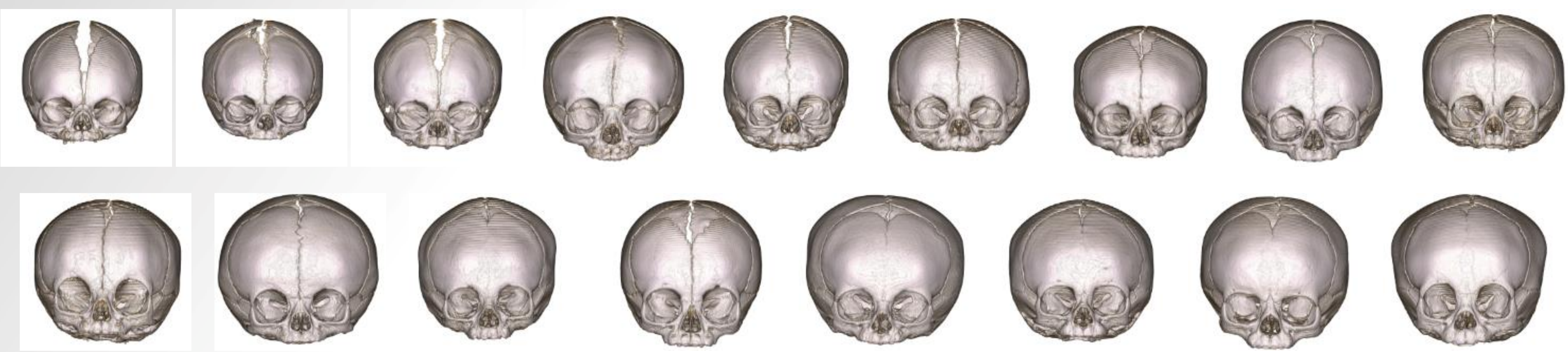


- Avants BB, Tustison NJ, Song G, Gee JC (2009) ANTS: open-source tools for normalization and neuroanatomy, *TransacMed Imagins Penn Image Comput Sci Lab.*
- Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC (2011) A reproducible evaluation of ANTs similarity metric performance in brain image registration, *Neuroimage* 54(3), 2033-2044.

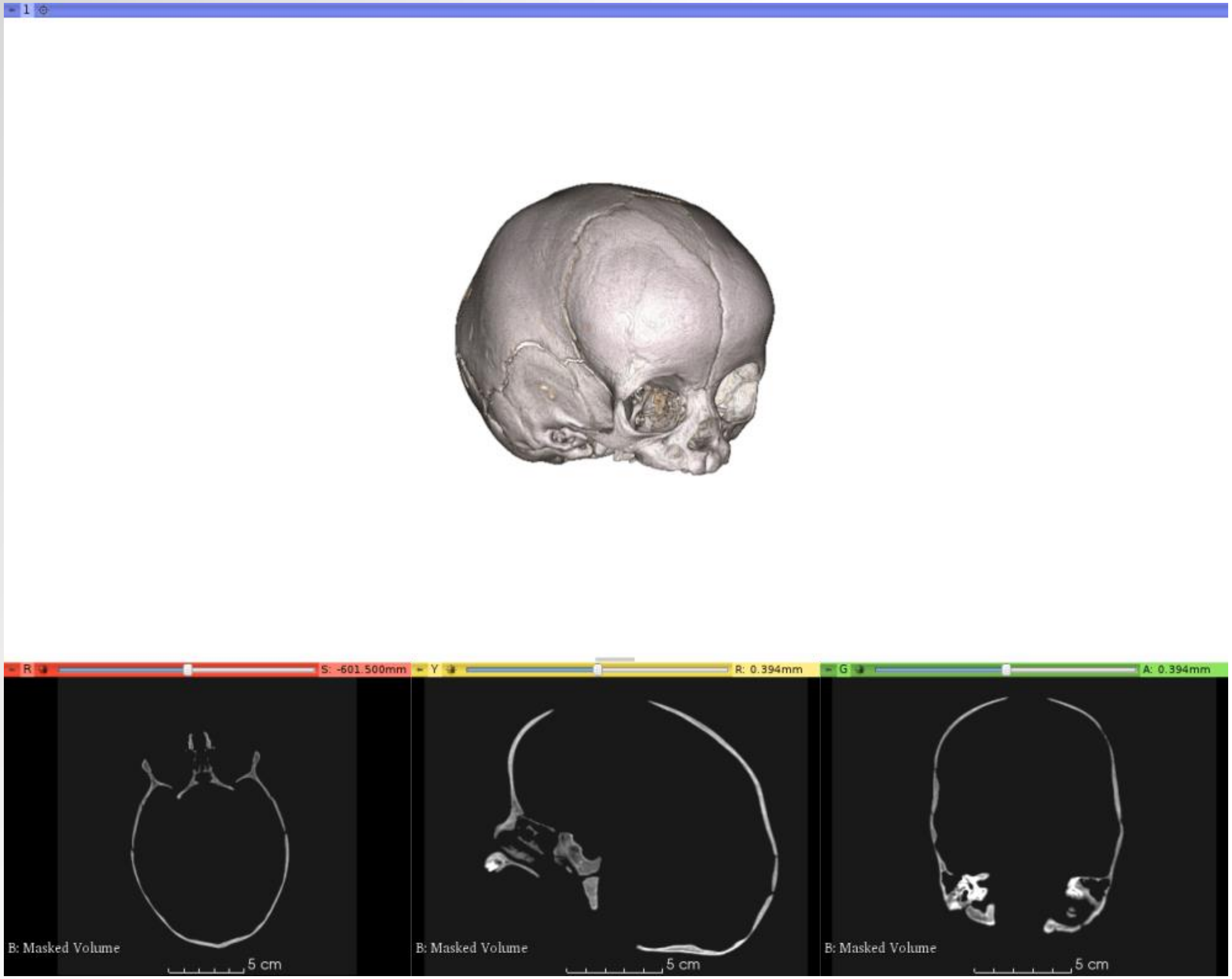
Data



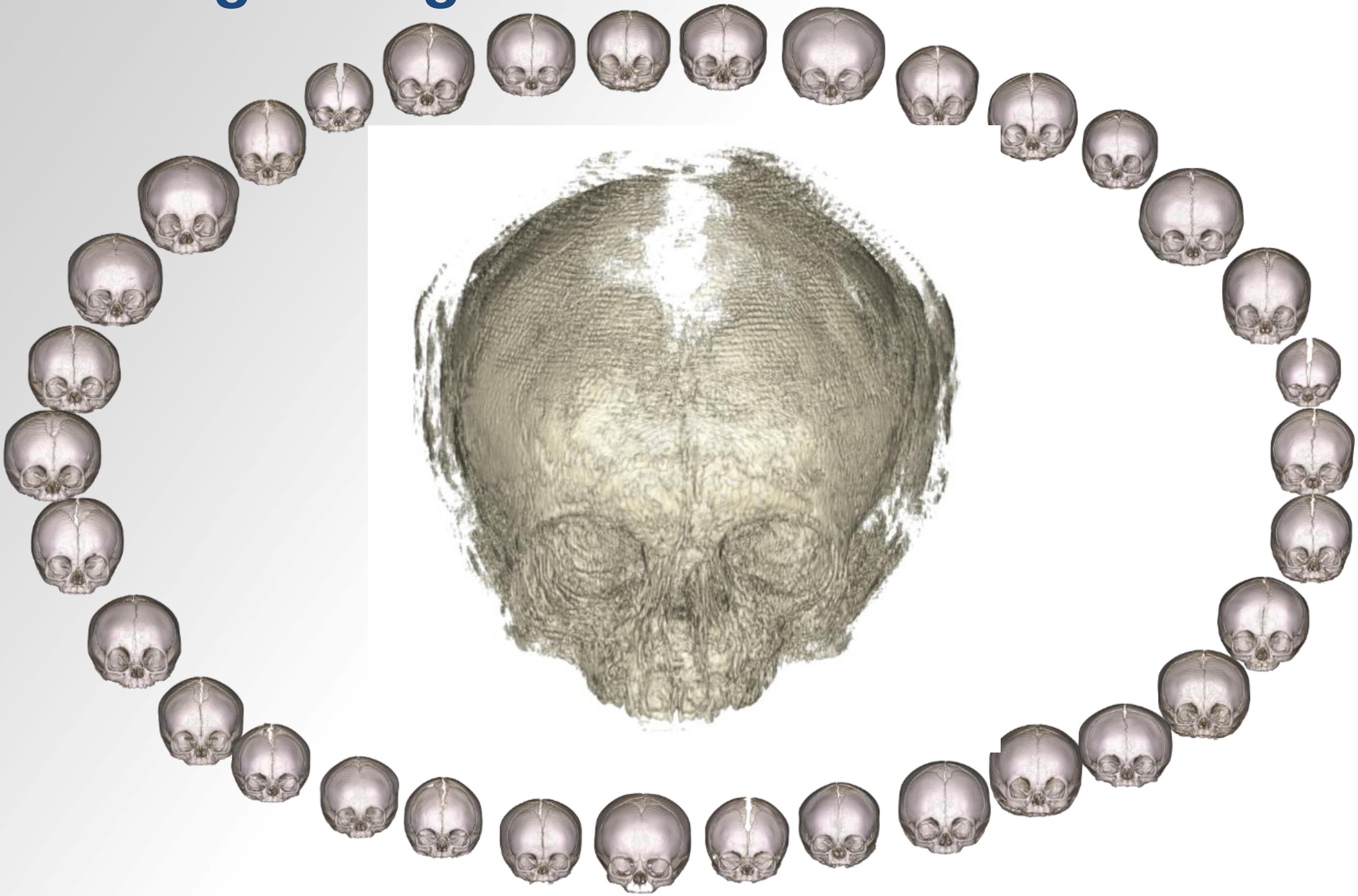
N = 34 normal samples (17 male and 17 female)
N = 81 sagittal CS samples (62 male and 19 female)
0-6 months old



Pre-processing

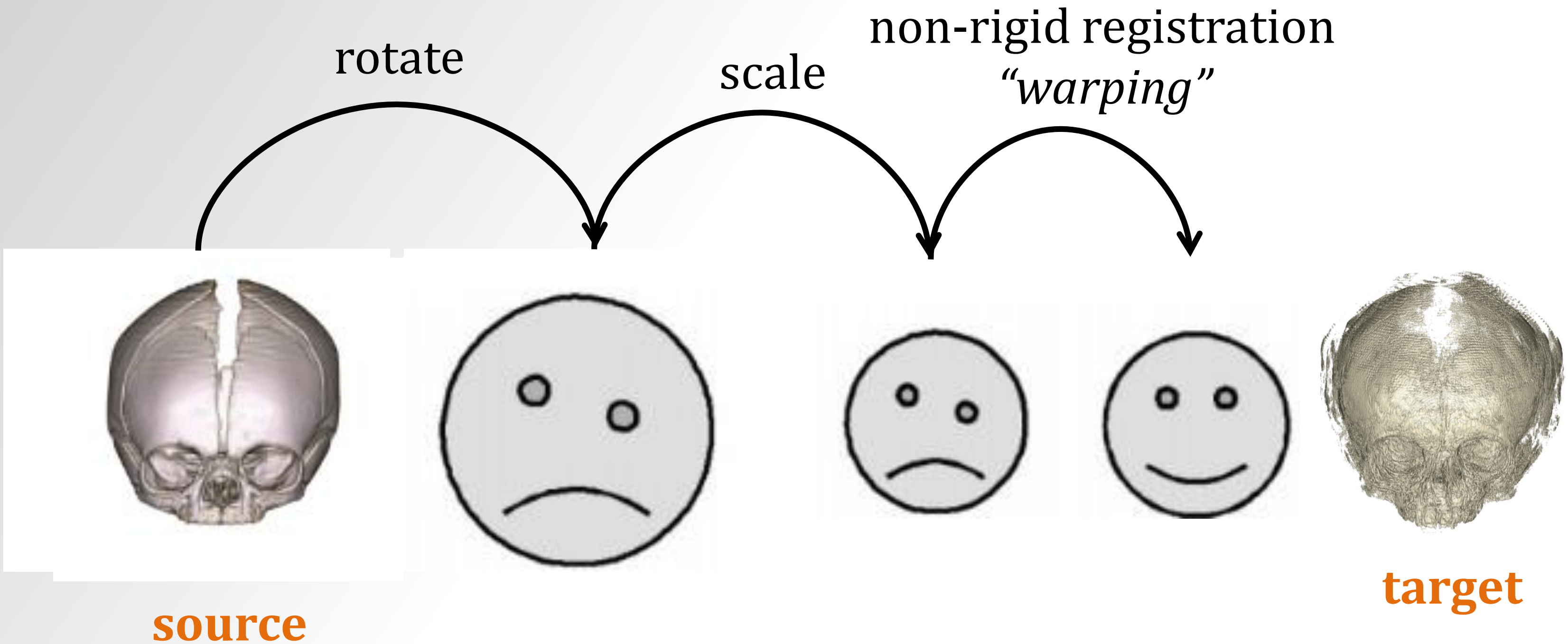


Average Image



Non-rigid Registration

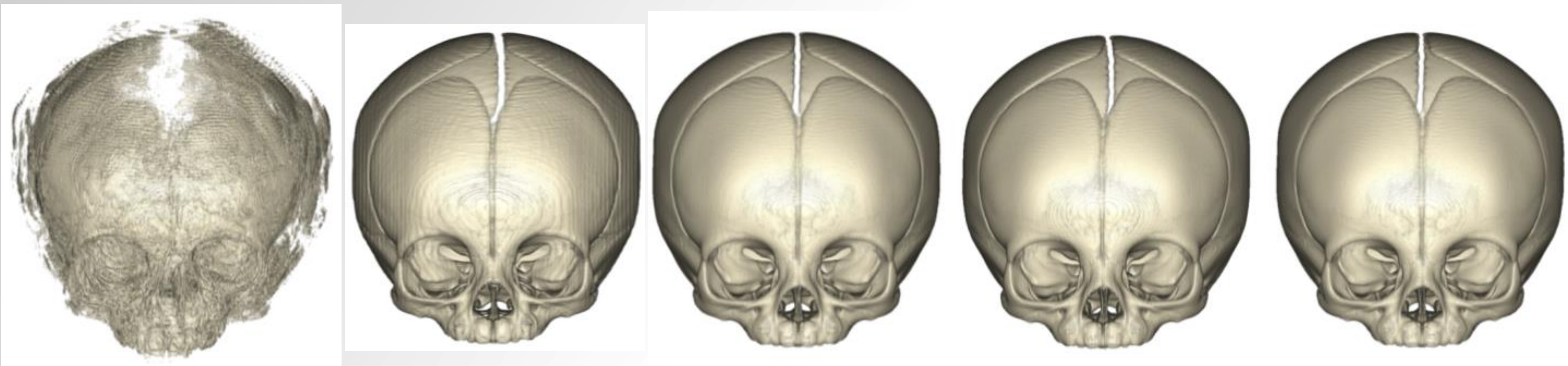
ANTs & ANTsR



Diffeomorphic registration: Symmetric Normalization (SyN) transformation

- Avants BB, Tustison NJ, Song G, Gee JC (2009) ANTS: open-source tools for normalization and neuroanatomy, *TransacMed Imagins Penn Image Comput Sci Lab.*
- Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC (2011) A reproducible evaluation of ANTs similarity metric performance in brain image registration, *Neuroimage* 54(3), 2033-2044.

Template Construction



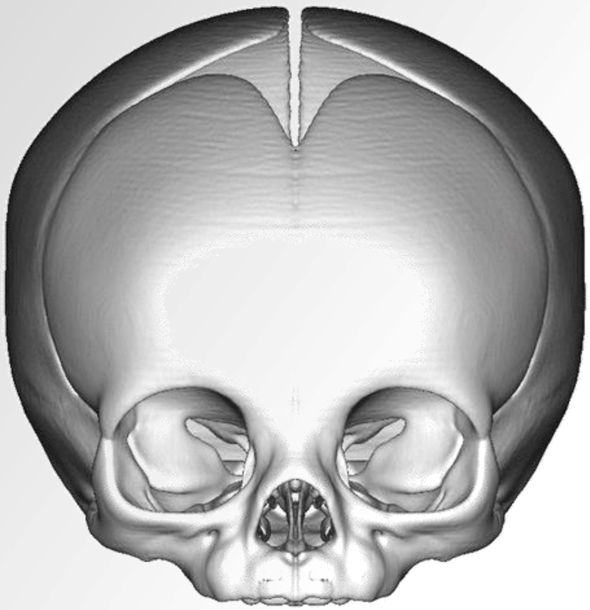
initial template | *1st iteration* | *2nd iteration* | *3rd iteration* | *4th iteration*

In each iteration:

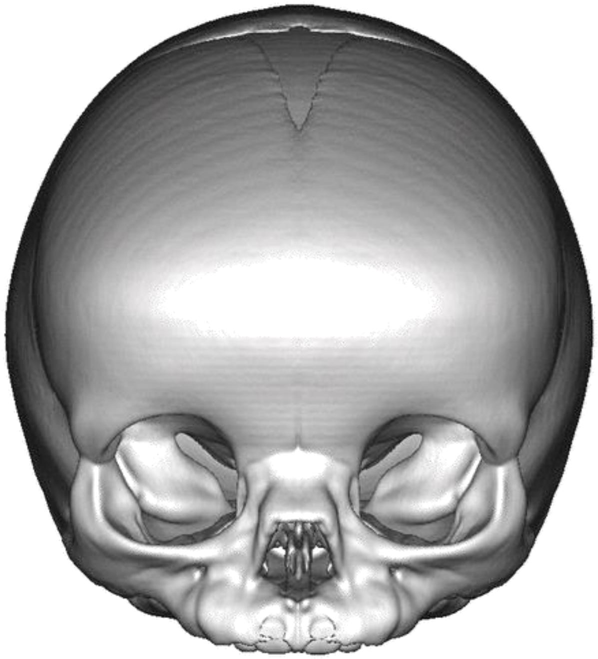
- Warp each sample to the current template
- Average warped images to create a new template
- Repeat until *convergence*

Population Templates

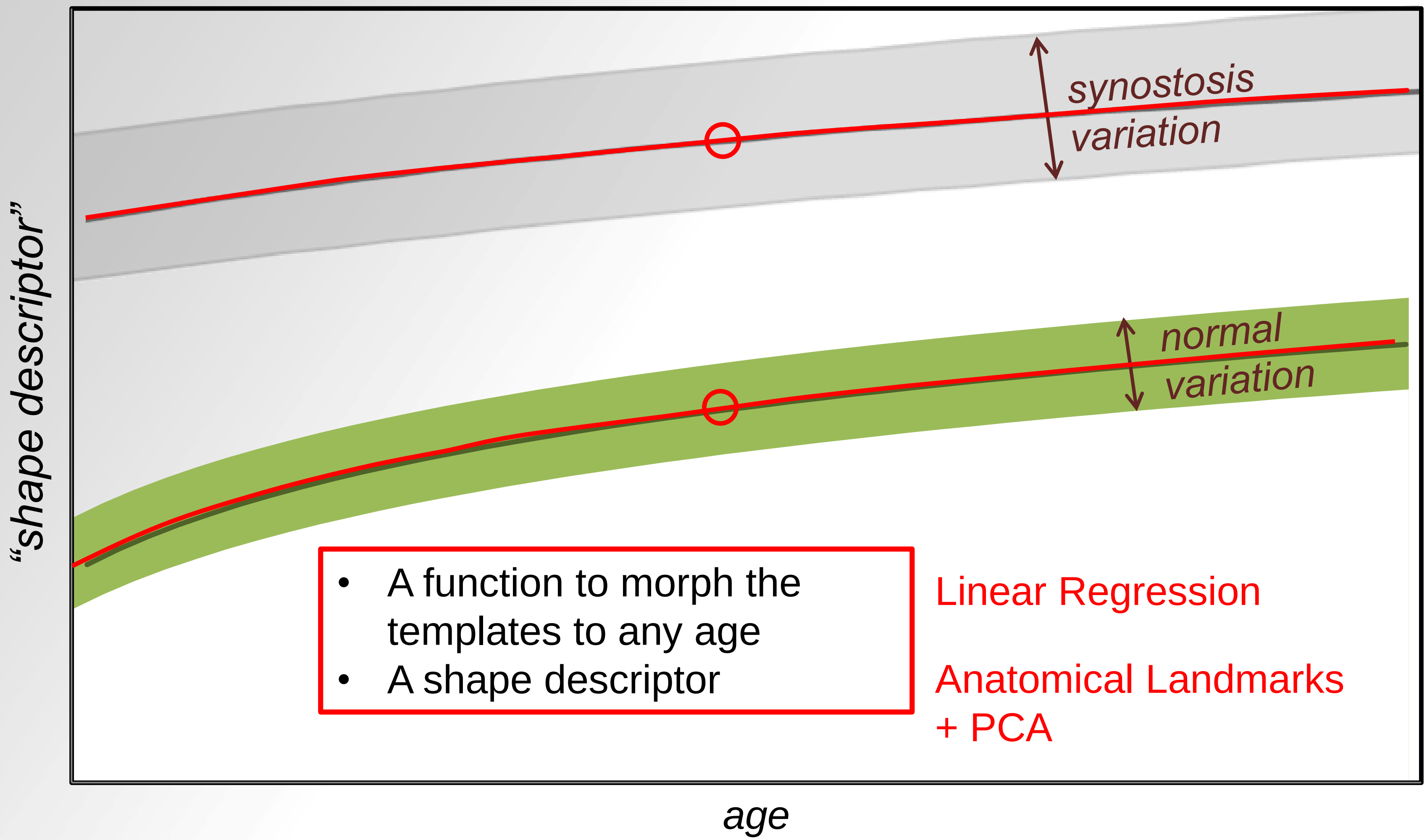
Normal Infant Template



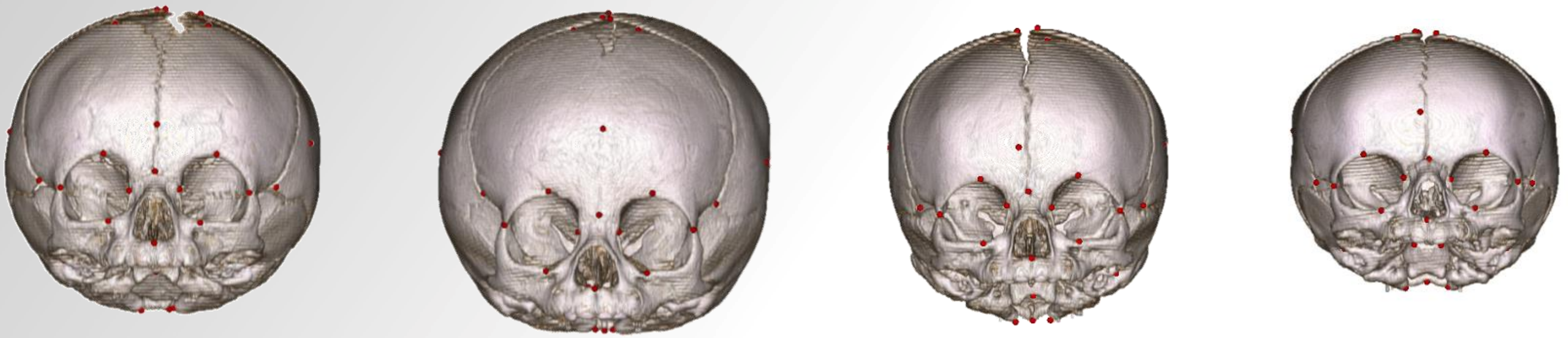
Sagittal CS Template



Hypothetical Growth



Growth Modeling



age_1 age_2 age_3 age_4

$$landmark.position \sim age + error$$

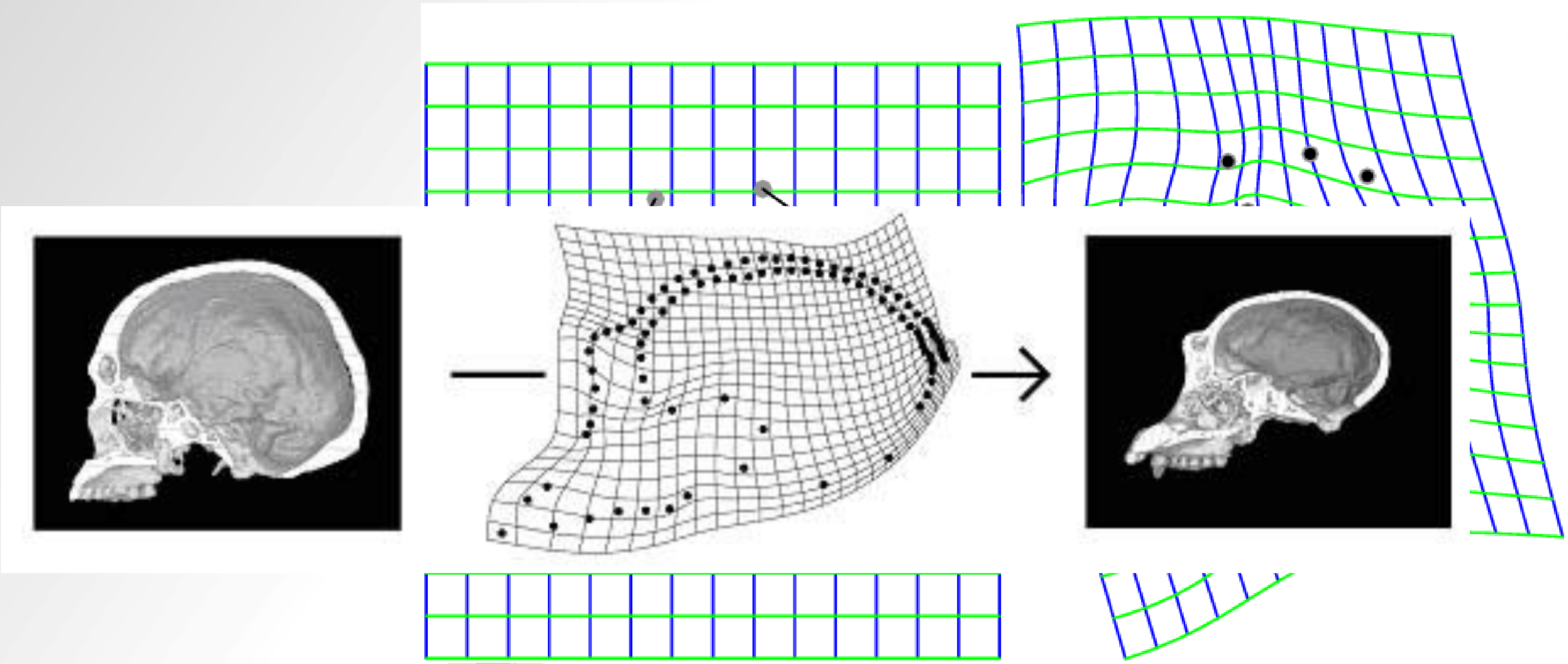
- We have 38 3D landmarks = $38 \times 3 = 114$ linear regression models.
- Landmark positions are not independent from each other.
- Principal Component Analysis

$$PC.scores \sim age + error$$

- PCA is also helpful with dimensionality reduction and noise removal.
- First 20 PCs explained 90% of the variation.

Thin Plate Splines

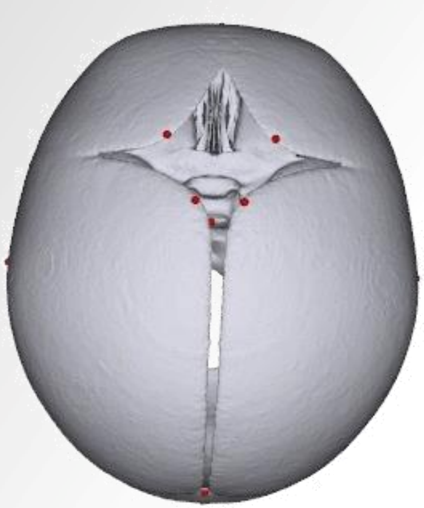
- It is an interpolation and smoothing technique.
- Using predicted landmark points, we *warp* the mesh.



- Bookstein, FL (1989) Principal Warps: Thin-Plate Splines and the Decomposition of Deformations, *IEEE Transactions on Pattern Analysis and Machine Intelligence* 11(6), 567-585.

Growth Models

Normal Infant Template



Sagittal CS Template

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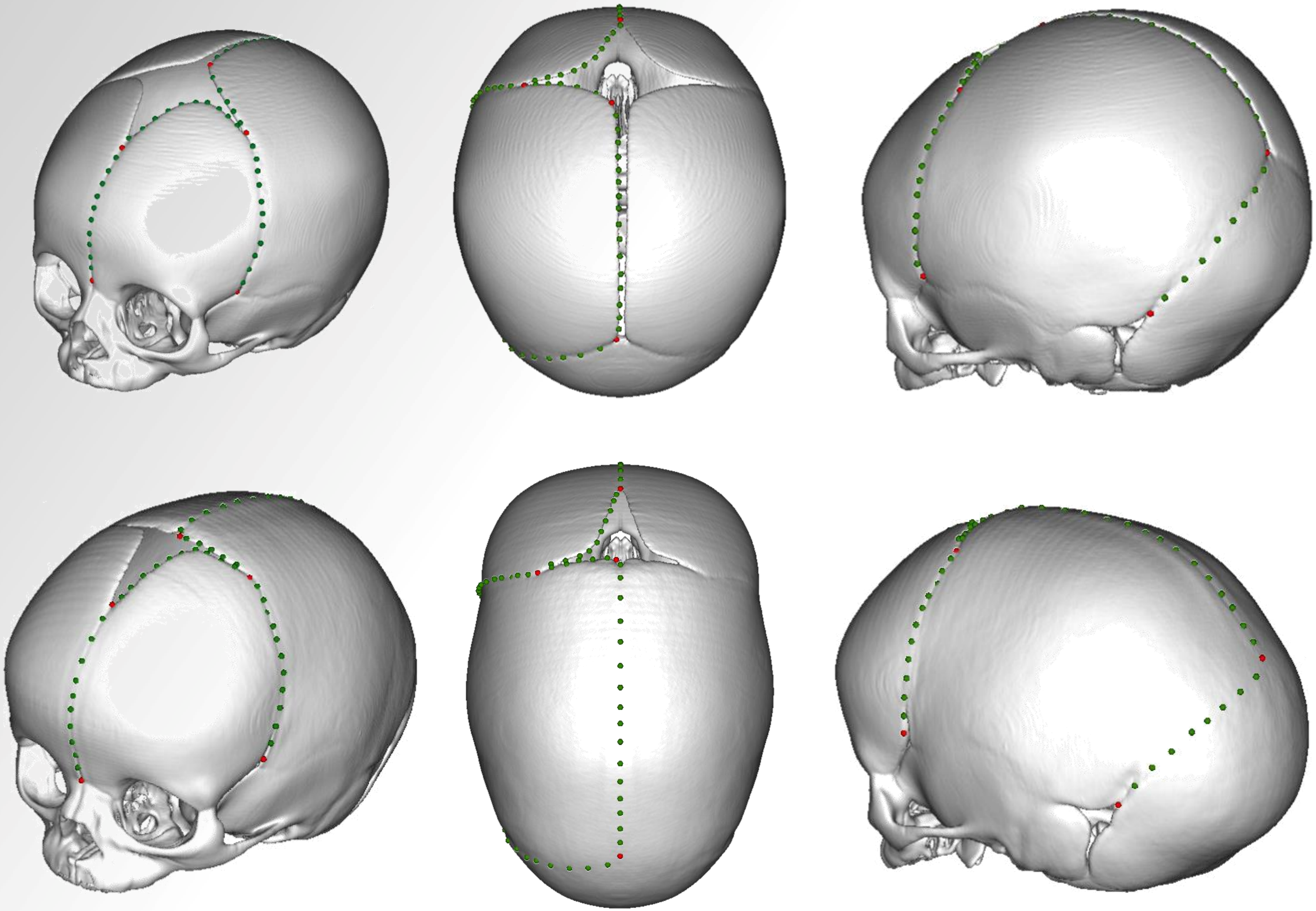
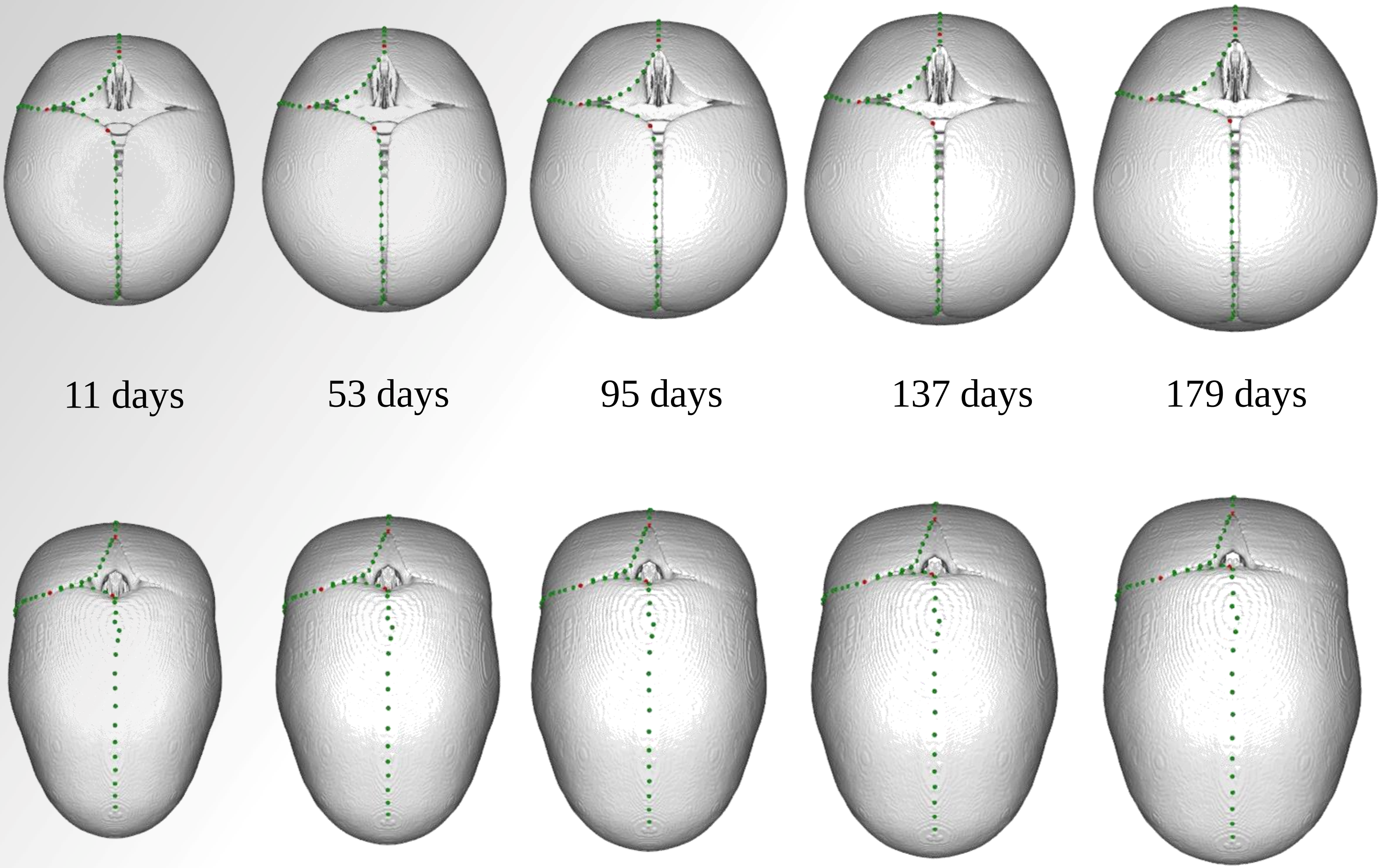
CRANIOFACIAL

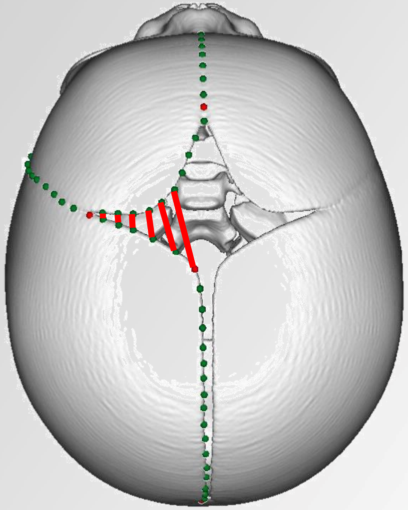
Suture Semi-landmarks

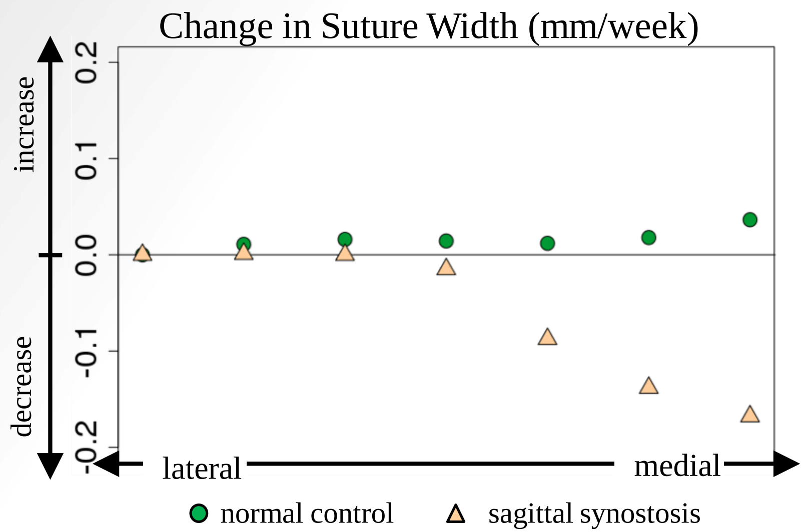


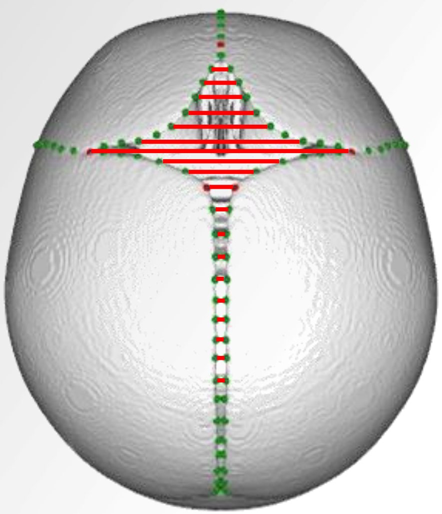
Suture Semi-landmarks

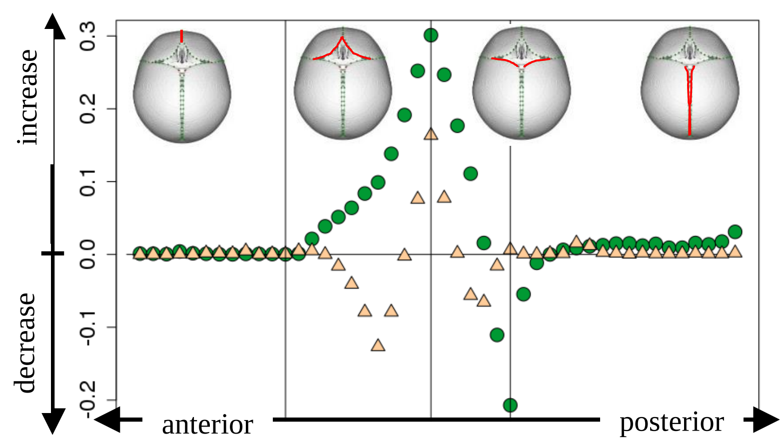


Suture Closure

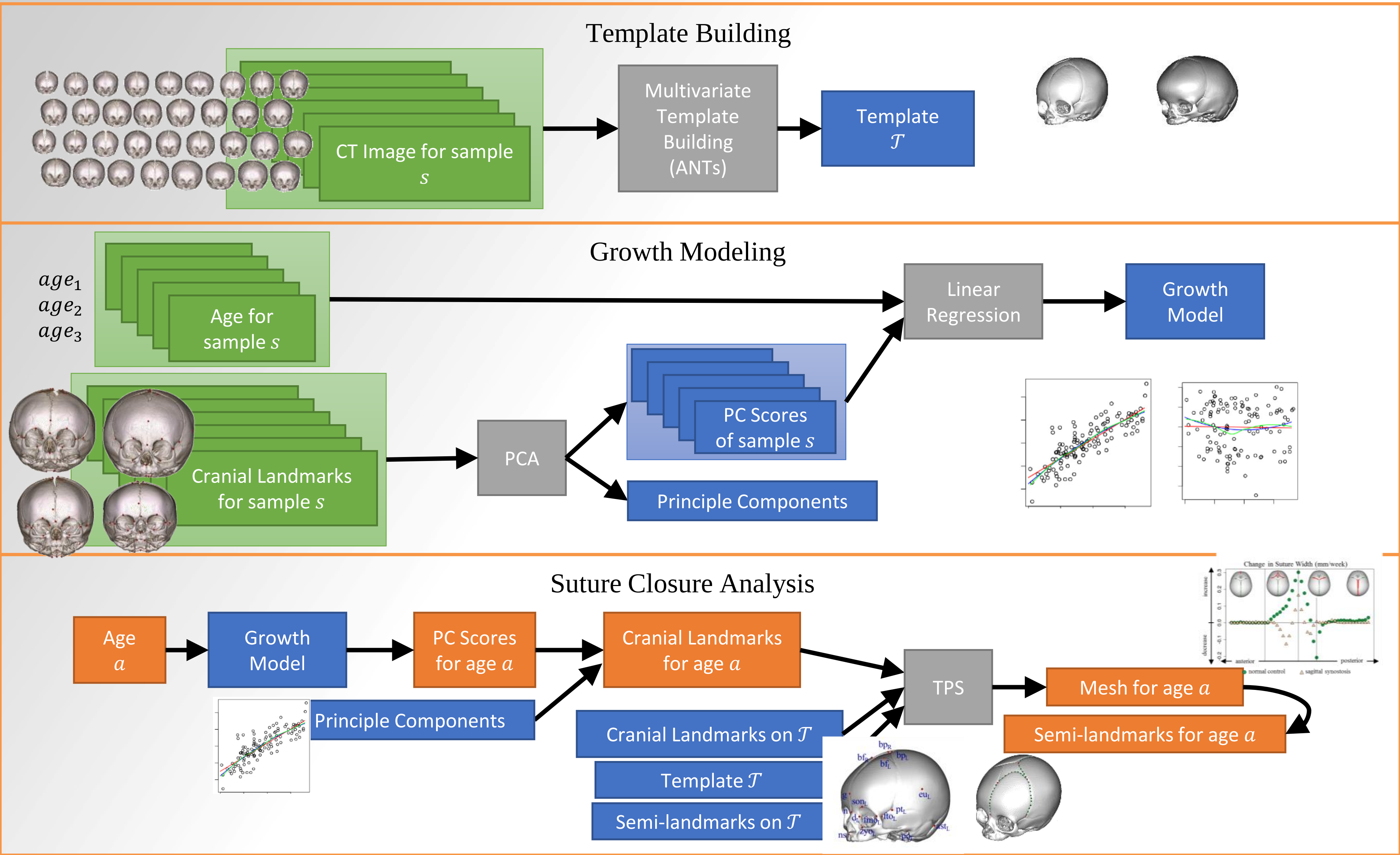








Recap

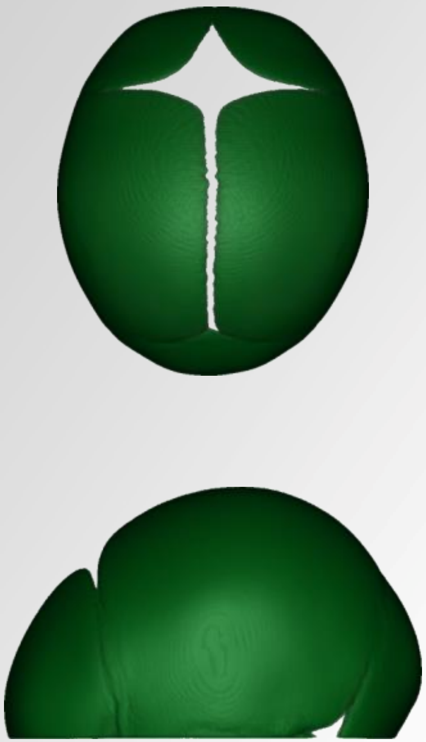


Template Building
CT Image for sample s
Multivariate Template Building (ANTs)
Template $\mathcal{T}$
Growth Modeling
age_1
age_2
age_3
Age for sample s
Cranial Landmarks for sample s
PCA
PC Scores of sample s
Principle Components
Linear Regression
Growth Model
Suture Closure Analysis
Age a
Growth Model
PC Scores for age a
Cranial Landmarks for age a
Principle Components
Cranial Landmarks on $\mathcal{T}$
Template $\mathcal{T}$
Semi-landmarks on $\mathcal{T}$
TPS
Mesh for age a
Semi-landmarks for age a
Change in Suture Width (mm/week)

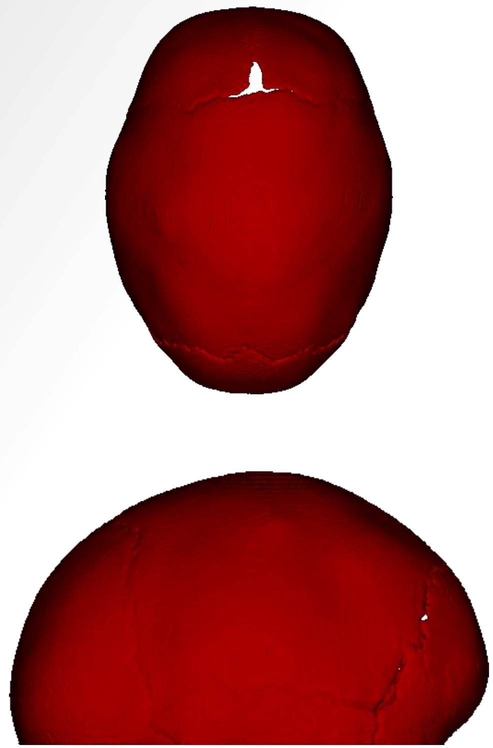
What else can you do with templates and diffeomorphic registration

BEYOND GROWTH

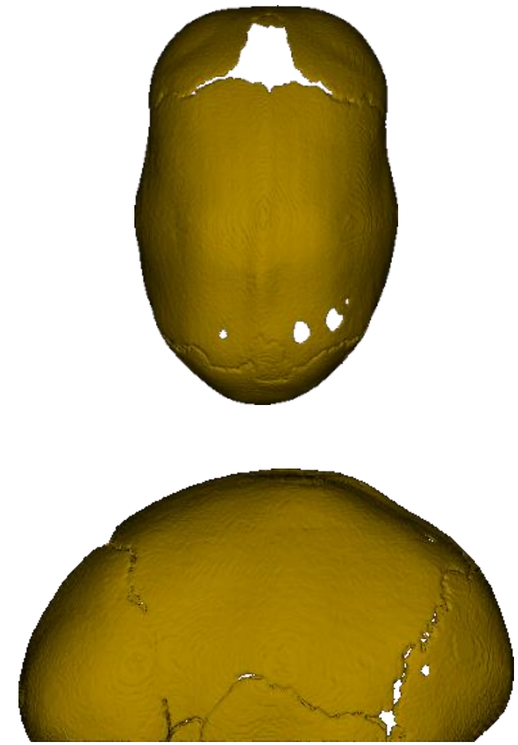
Shape Description



normal template

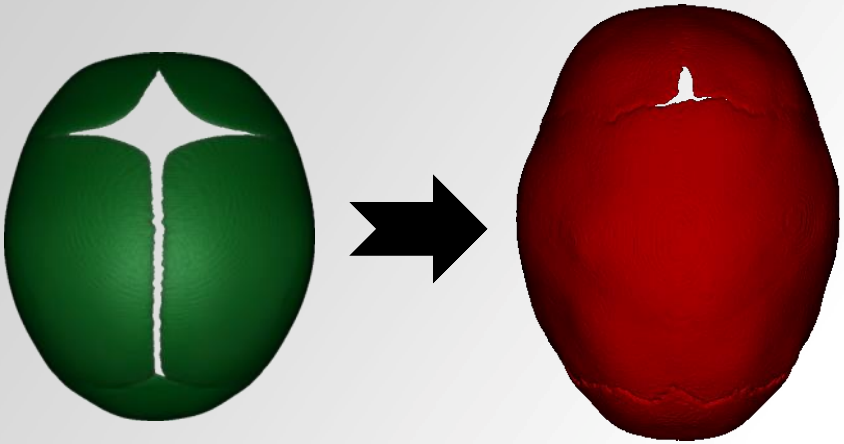


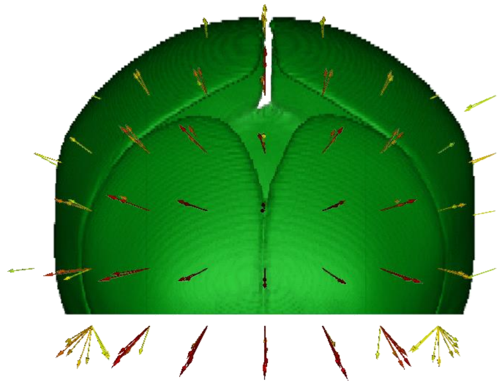
sagittal sample1

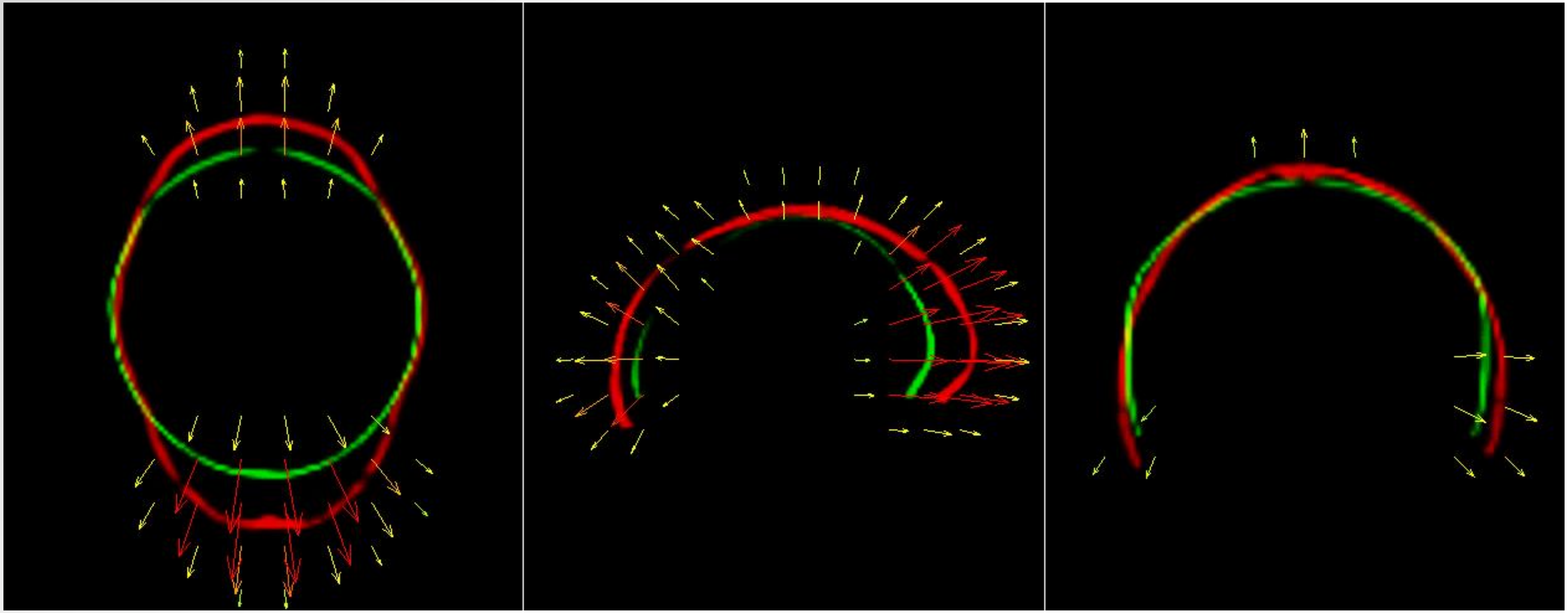


sagittal sample2

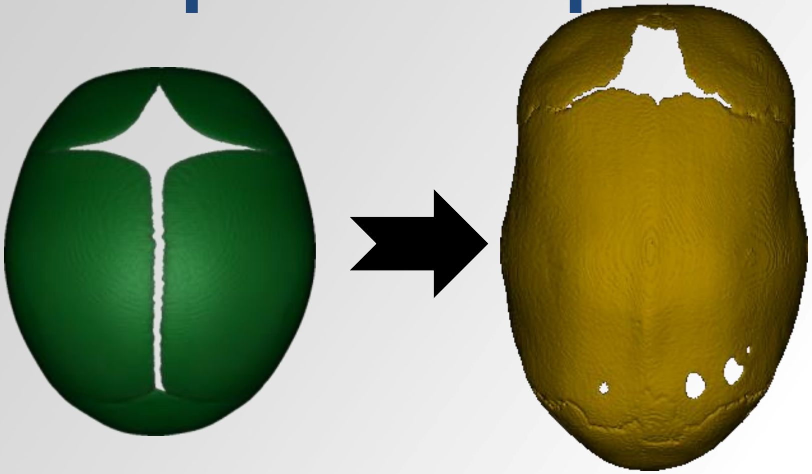
Shape Description

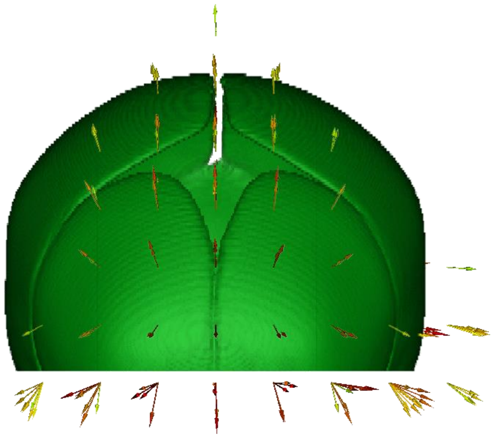


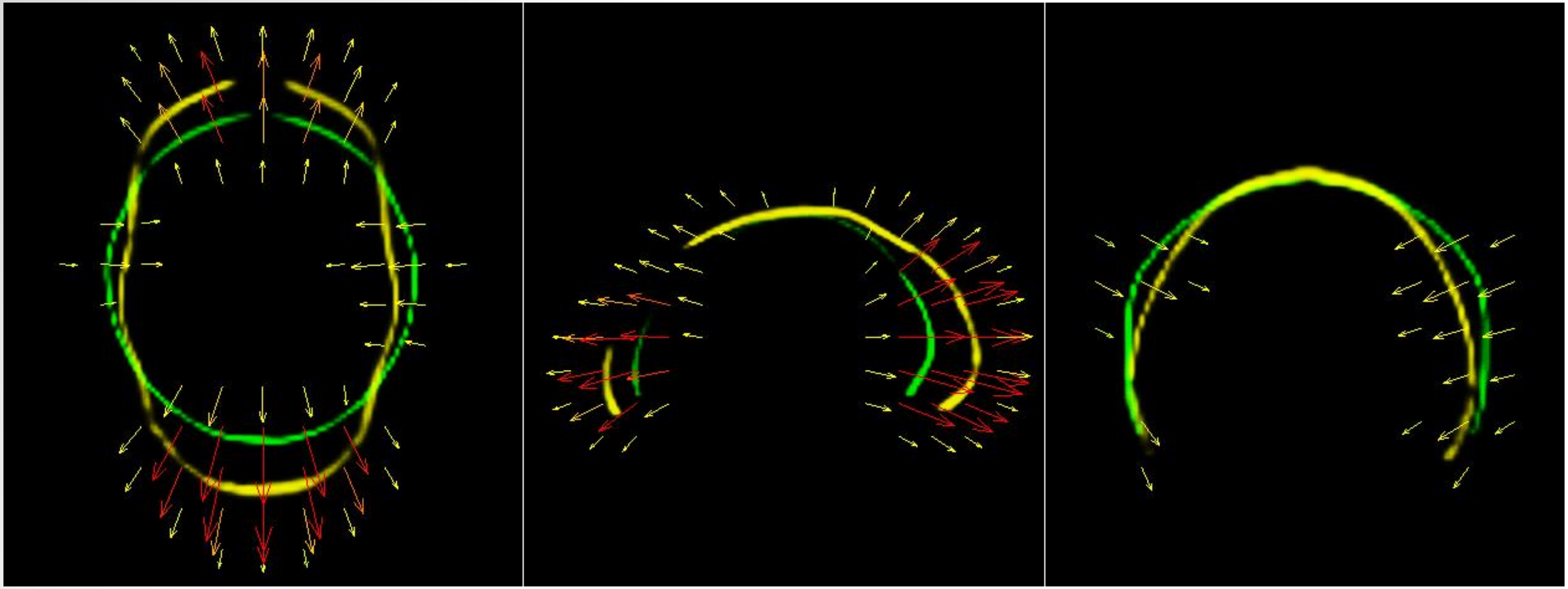




Shape Description







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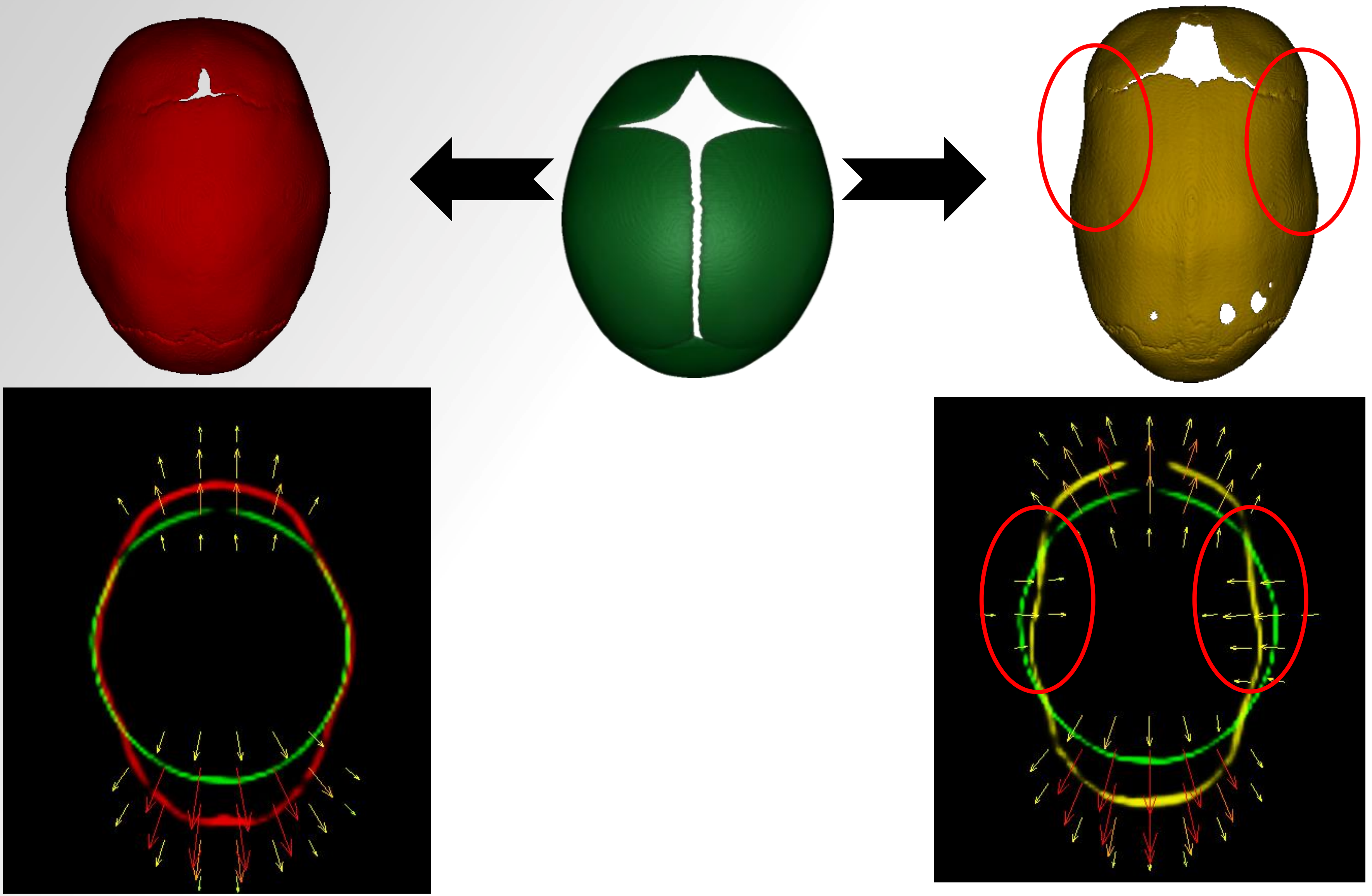

Challenges and Pitfalls

- Data acquisition methods
  - CT, MRI, X-rays, fMRI
  - 3D stereophotogrammetry, laser scanning
- Data format
  - Volumes vs meshes
  - Data loss vs simplification
- Tools
  - Biological correspondence vs full automation
  - Look under the hood
  - Sample size

Papers of Interest

1. Mercan E, Hopper R, Maga AM. Cranial Bone Growth in Isolated Sagittal Craniosynostosis Compared to Normal Growth in the First Six Months of Age. *bioRxiv*. 2019;528869(1):21. doi:1037//0033-2909.I26.1.78
2. Flaherty K, Singh N, Richtsmeier JT (2016) Understanding craniosynostosis as a growth disorder, *Wiley Interdiscip Rev Dev Biol* 5(4), 429-459.
3. Li Z, Park BK, Liu W et al. (2015) A statistical skull geometry model for children 0-3 years 579 old, *PLoS ONE* 10(5).
4. Andresen PRø, Bookstein FL, Conradsen K, ErsbØll BK, Marsh JL, Kreiborg S. Surface-bounded growth modeling applied to human mandibles. *IEEE Trans Med Imaging*. 2000;19(11):1053-1063.
5. Herlin C, Largey A, DeMatteï C, Daurès JP, Bigorre M, Captier G. Modeling of the human fetal skull base growth: Interest in new volumetrics morphometric tools. *Early Hum Dev*. 2011;87(4):239-245.
6. Libby J, Marghoub A, Johnson D, Khonsari RH, Fagan MJ, Moazen M. Modelling human skull growth: a validated computational model. *J R Soc Interface*. 2017.

7. Avants BB, Tustison NJ, Song G, Gee JC (2009) ANTS: open-source tools for normalization and neuroanatomy, TransacMed Imagins Penn Image Comput Sci Lab.
8. Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC (2011) A reproducible evaluation of ANTs similarity metric performance in brain image registration, Neuroimage 54(3), 2033-2044.
9. Fedorov A, Beichel R, Kalpathy-Cramer J, et al. 3D Slicer as an image computing platform for the Quantitative Imaging Network. *Magn Reson Imaging*. 2012;30(9):1323-1341. doi:10.1016/j.mri.2012.05.001

Software

- 3D Slicer https://www.slicer.org/
  - A platform for all: Simple GUI editor/viewer, Python API for extensions and custom analysis
  - An excellent software for all level users/developers
- ANTs/ANTsR http://stnava.github.io/ANTs/
  - Registration toolkit: developed by neuroscientists for brain MRIs but works great with a bunch of modalities, 2D/3D/4D
  - Available as command-line tools, C++ and R - Python in progress
- FSL https://fsl.fmrib.ox.ac.uk/fsl/fslwiki
  - An older competitor of ANTs from Oxford, from the same people who did FreeSurfer
- VTK https://vtk.org/
  - Visualization toolkit, great library for mesh (surface model) processing
- ITK and SimpleITK https://simpleitk.org/
  - Image analysis (CT/MRI etc.) toolkits, available in C++, R, Python.