Voxel-wise T2 relaxometry of Normal Pediatric Brain Development in 326 datasets of 114 healthy infants and toddlers

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Outline

- Motivation: reasons to study T_2 relaxometry in children
- Image processing problems
- Pediatric anatomical templates
- T_2 relaxometry
- Inter-subject co-registration
- Inter-subject T_2 age regression
- Validation
- Discussion

Motivation

- T1w contrast between the grey and white matter is reversed during the first 4-6 months
- The same is true for T2w contrast up to 9-10 months
- These changes are related to myelination and change in water contents
- The actual timing depends on many factors (sequence, hardware)
- The goal of this study is to perform quantitative voxel-wise analysis of maturation throughout the brain using T_2 relaxometry in a common stereotactic coordinate system

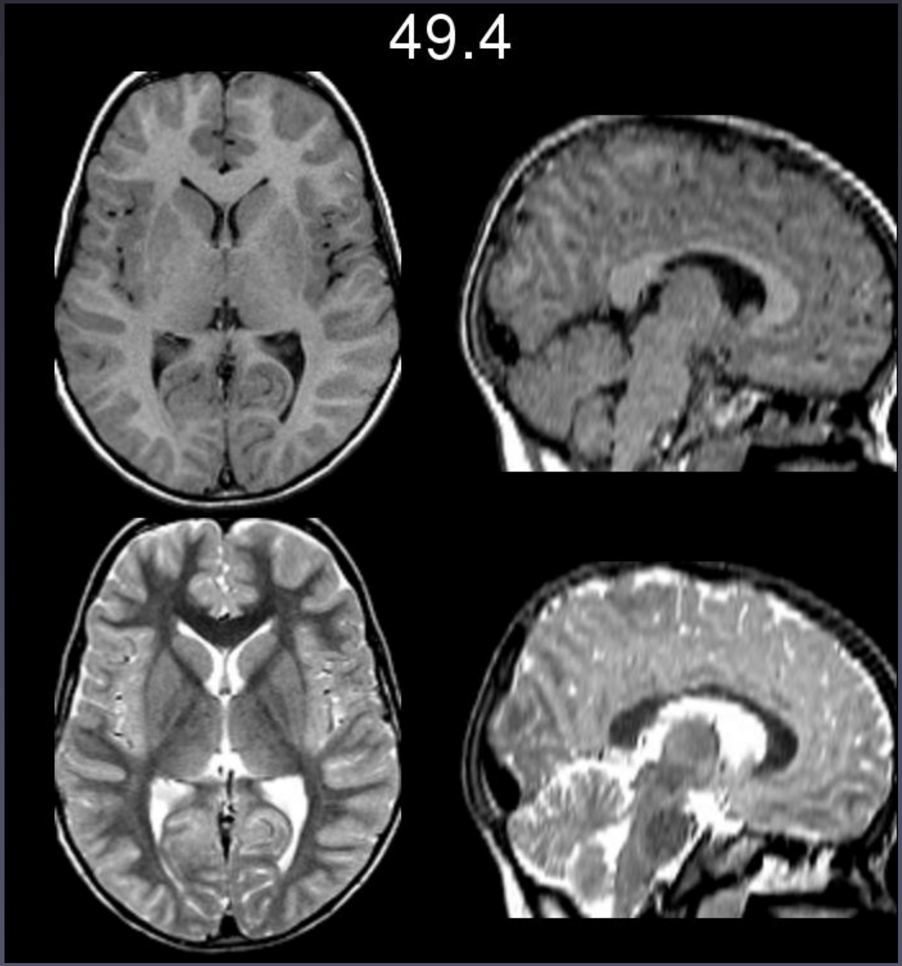
Image processing problems

- During the first year of life shape of the brain changes very fast
- The contrast in T1w and T2w images also changes very fast
- The assumption about three tissue classes separable on T1w or T2w doesn't work for developing brain
- Scans currently available for the study have low resolution (1x1x3mm)

Pediatric images

T1w

T2w



Possible solution

- Develop age specific templates to facilitate image processing using existing tools
- Develop more robust image registration tools using mutual information (MI) cost function for non-linear registration

Template building

1. Given J_k – the template, for each scan I_i calculate $X_{i,k}$ – mappings from the template to a scan, using the $Y^{-1}_{i,k-1}$ (inverse corrected mappings) from the previous iteration as a starting point (use identity for the first iteration)

$$X_i = \arg\min_x \int_{volume} \left(J\left(X_i(v)\right) - I_i(v)\right)^2$$

2. Calculate the mean shift of the current template

$$X_{0,k} = x + \sum_n h_i(x) \Big/ n$$

3. Calculate corrected inverse mappings $Y^{-1}_{i,k}$, Apply corrected inverse mappings to individual subjects and generate an average which will be used as a new template:

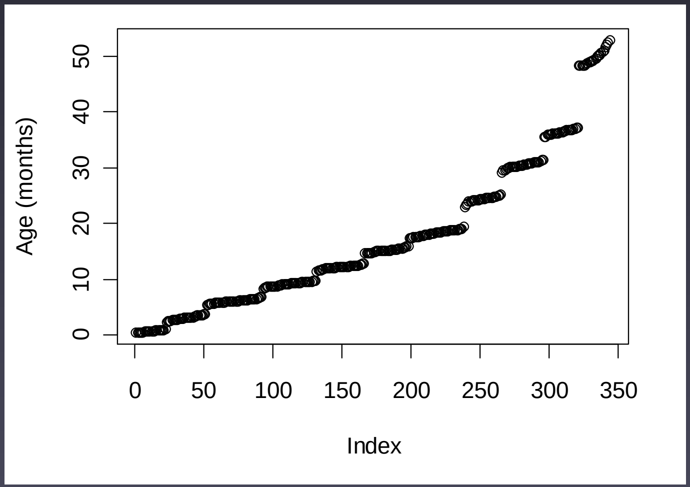
$$J_{k+1}(x) = \sum_n I\left(Y_{i,k}(x)\right) \Big/ n$$

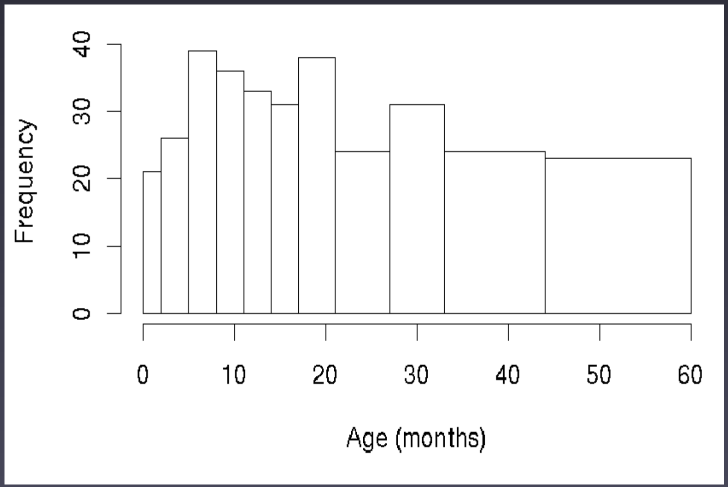
4. Repeat from step 1, until convergence is reached

Miller, M., A. et al. Statistical methods in computational anatomy. Stat Methods Med Res **6**(3): 267-99 1997.

Guimond, A. et al. Automatic Computation of Average Brain Models. Medical Image Computing and Computer-Assisted Interventation — MICCAI'98**:** 631.

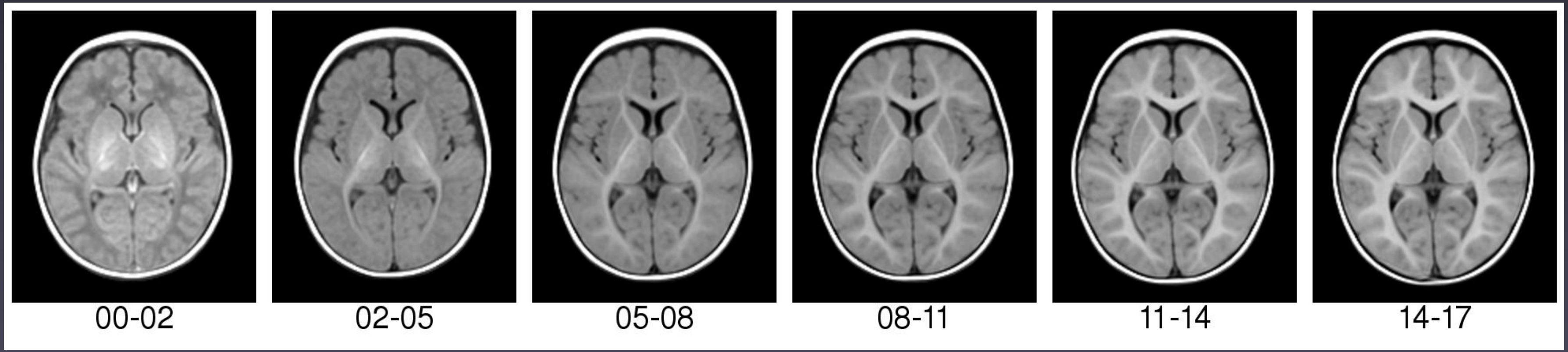
NIHPD objective 2 database

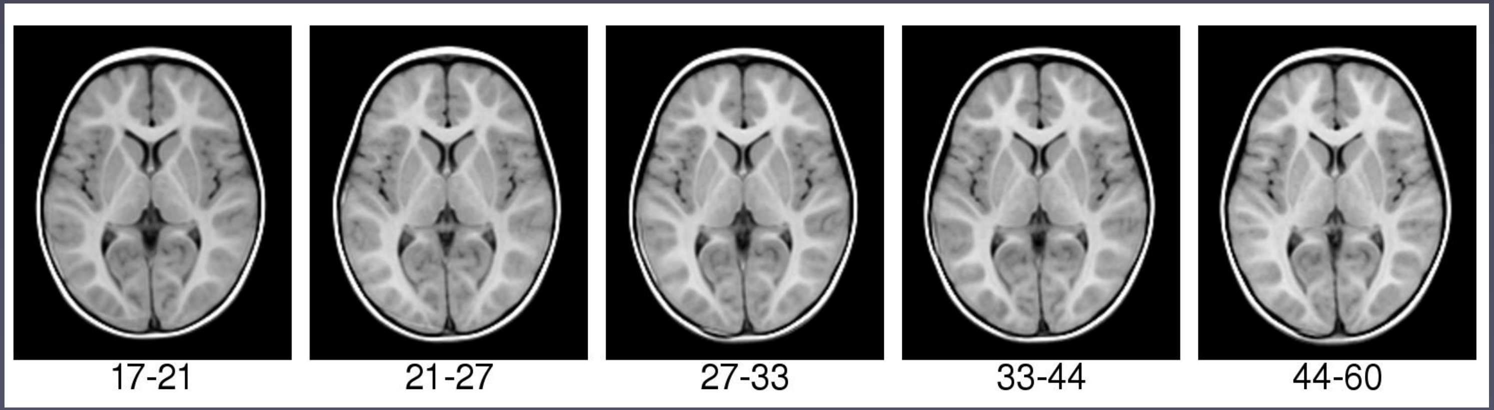




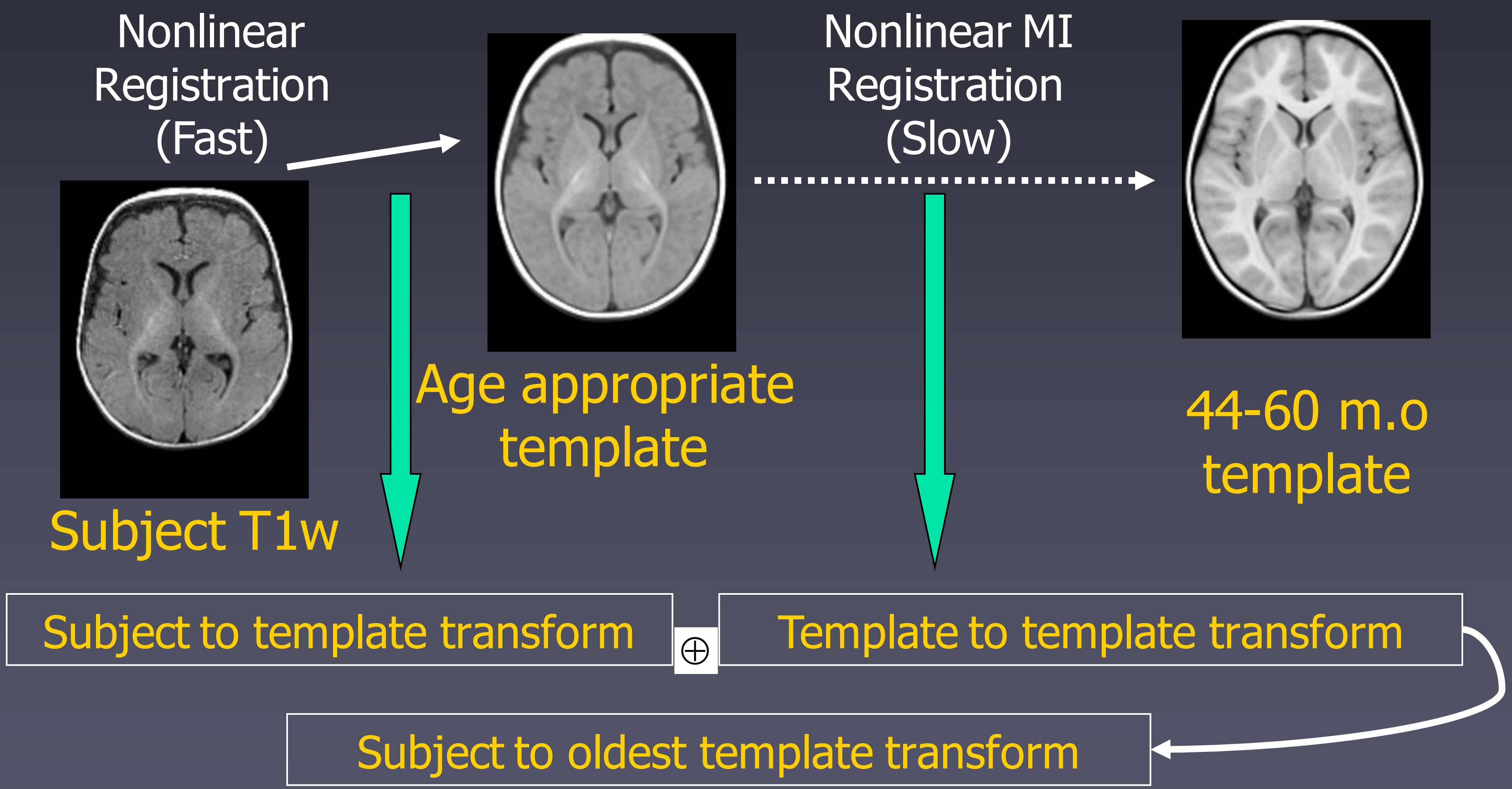
- 114 normal healthy children
- total of 346 datasets
- Each dataset included one multislice T1w scan (TR=500ms TE=12ms) and a multislice dual echo PDw/T2w scan (TR=3500ms, TE=14,112ms)
- Some datasets included an additional acquisition of dual echo scans with longer TE=83,165ms

Pediatric templates





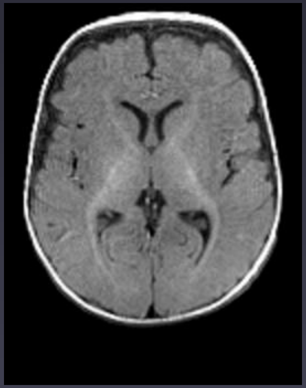
Inter-subject co-registration



Voxel-wise T_2 relaxometry

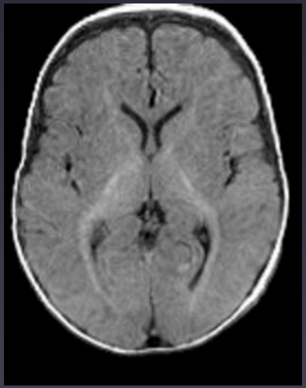
- All dual-echo scans registered to T1w scan linearly (rigid body) using MI cost function
- Voxel-wise linearized regression performed to estimate T_2:
  $ln(S_i)=ln(S_0)-TE_i/T_2$
  S_0 equilibrium signal
  S_i signal corresponding to echo time TE_i

Inter-subject co-registration

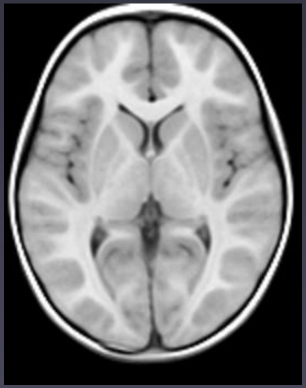


Subject T1w

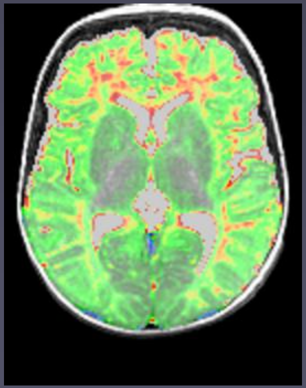
Resampling →



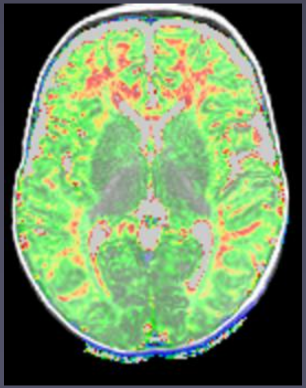
T1w



44-60 m.o template



Subject T_2

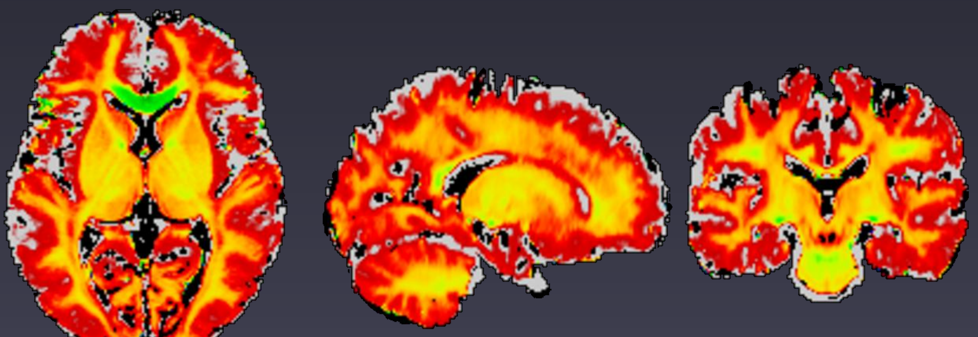


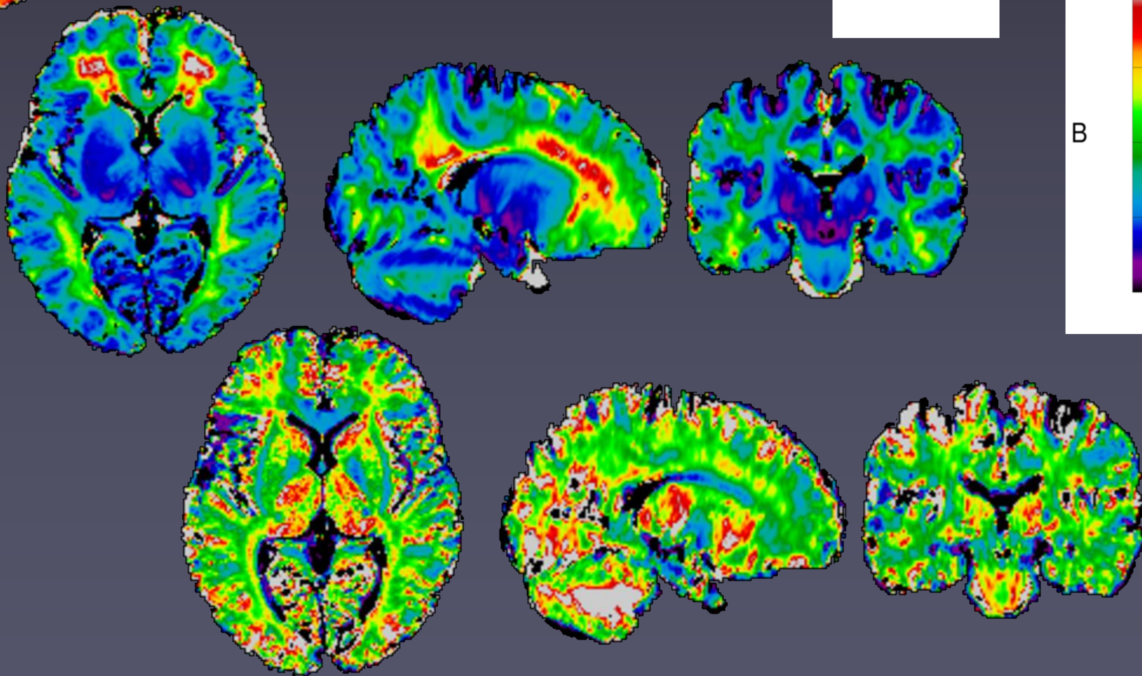
T_2

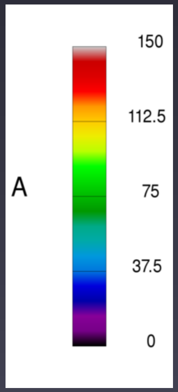
Inter-subject T_2 regression

- Regressions of T_2 over age were performed in a voxel-by-voxel fashion using all images that passed QC
- A mono-exponential $T_2=A+B*exp(-t*C)$ model was used
- For the sake of presentation we calculated the age at which T_2 reaches 160ms (maturation for WM)

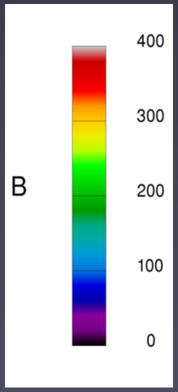
T_2 regression results

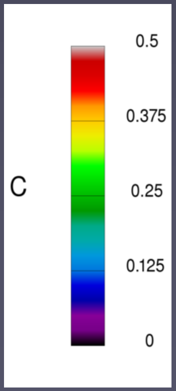




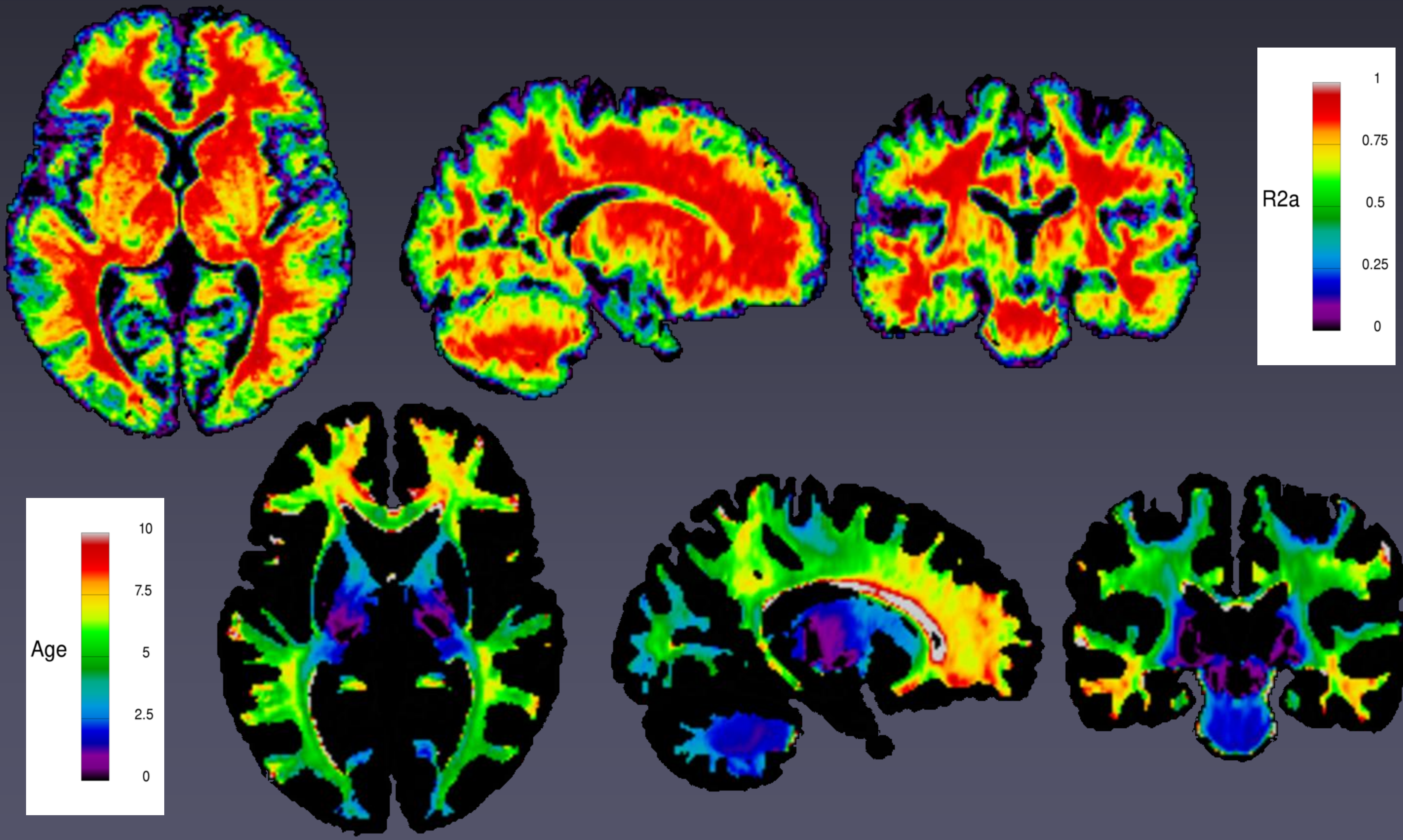


$T_2=A+B*exp(-t*C)$





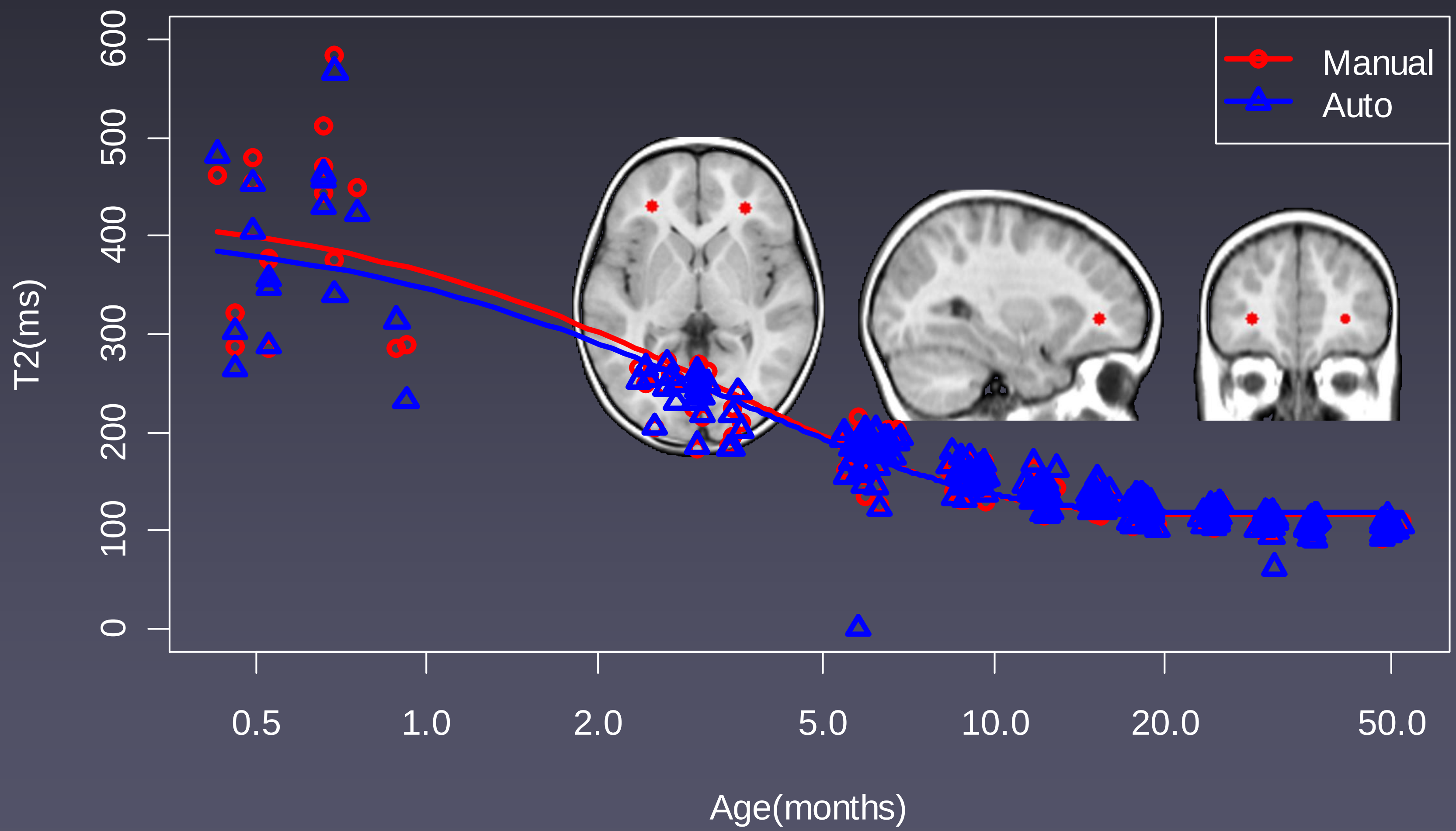
T_2 regression results



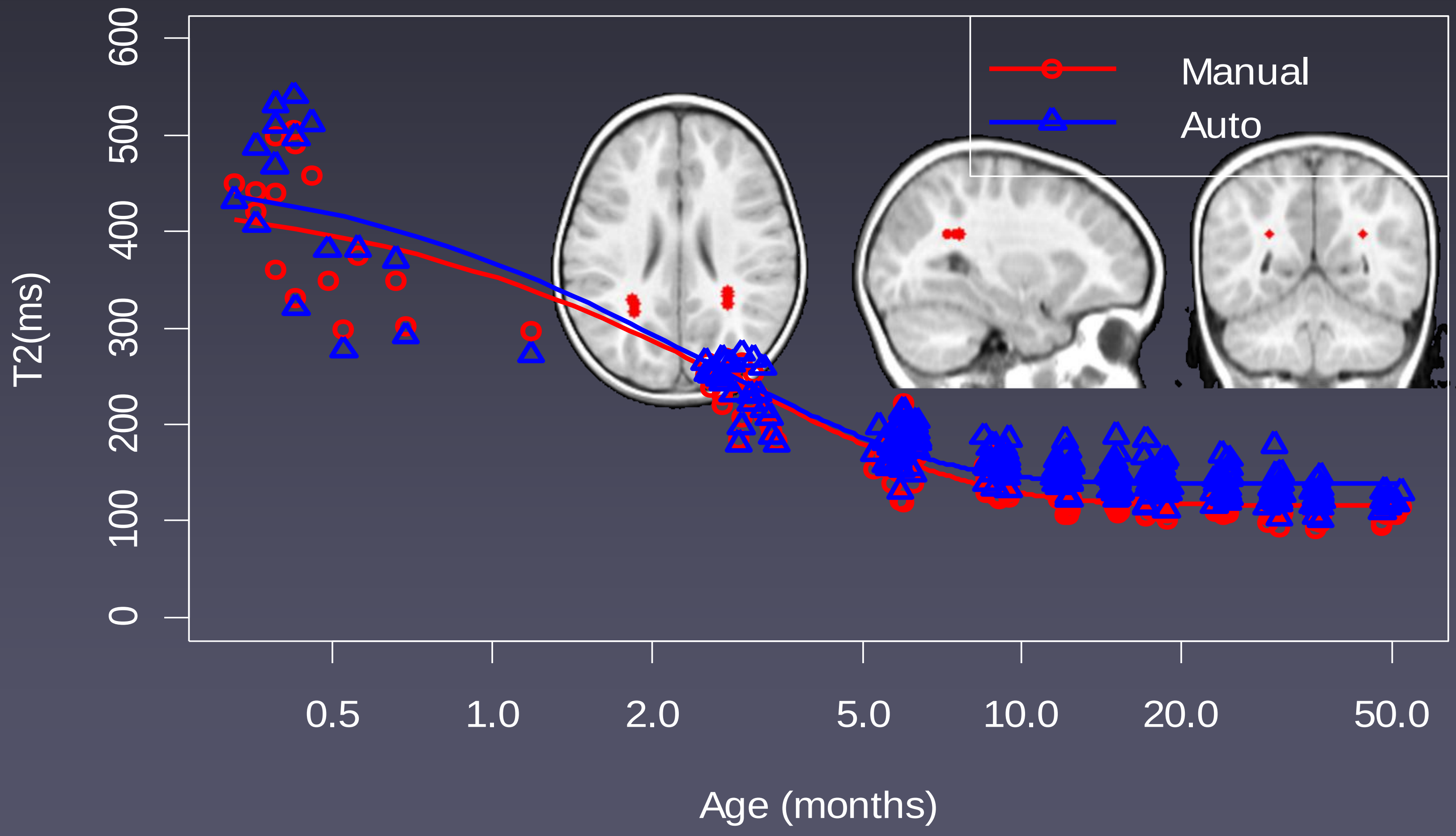
Validation

- Human rater manually identified several anatomical regions of interest (ROI) on the native (unprocessed) images and calculated corresponding T_2
- These values where then were compared to the T_2 values extracted using ROIs defined on the average anatomical template of 44-60 m.o

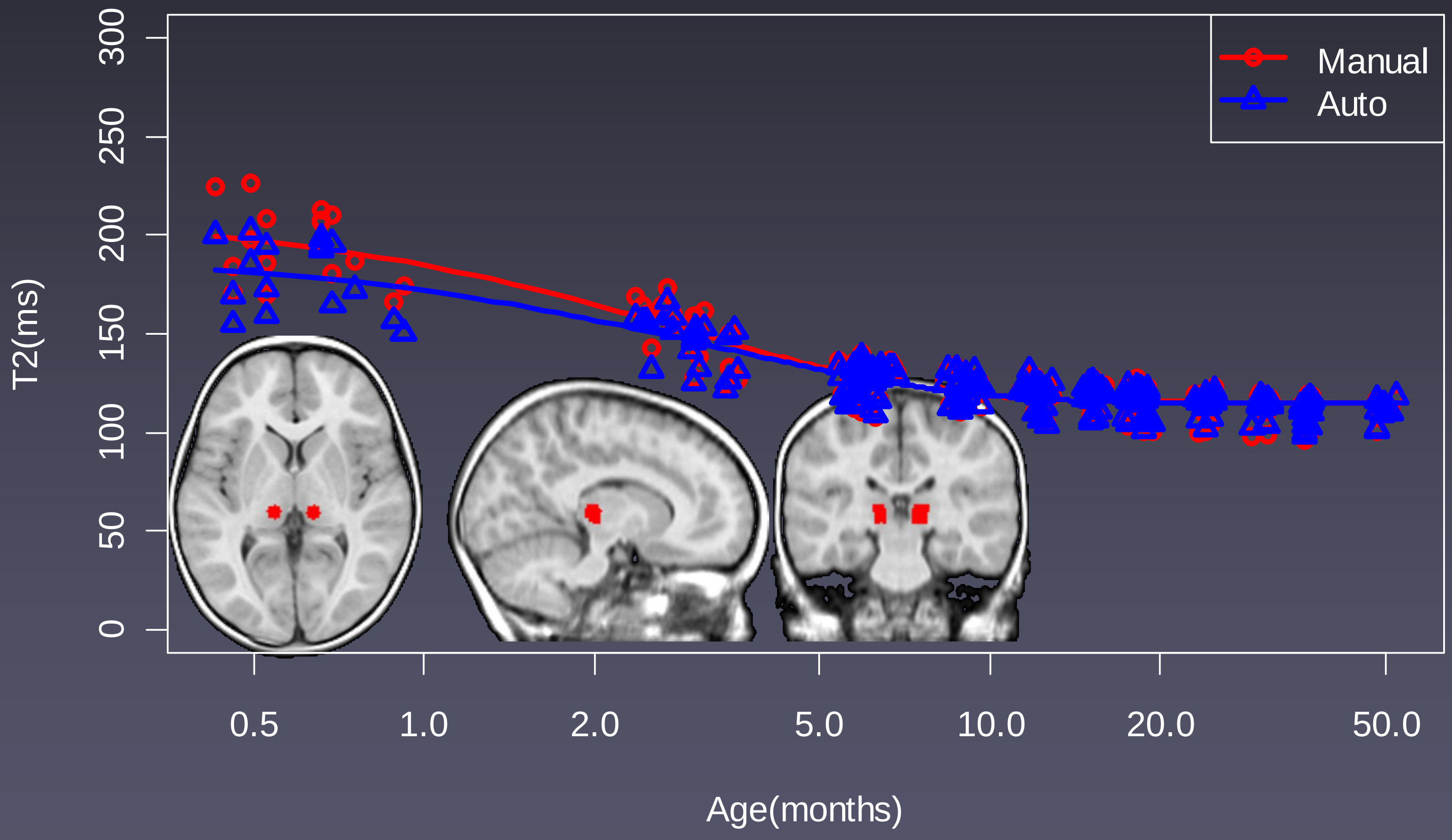
Minor forceps



Occipital WM



Thalamus



Manual
Auto
T2(ms)
0
50
100
150
200
250
300
0.5
1.0
2.0
5.0
10.0
20.0
50.0
Age(months)

Discussion

- Our results are consistent with the results of our manual ROI based technique with the exception of small bias in Occipital WM ROI
- In general, our findings are consistent with the known white matter maturation pattern
- The R^2 (coefficient of determination) map indicates that regression is able to explain 95% of inter-subject variability of T_2 within the bulk of the white matter, and fails in the peripheral gray matter and near the edge of ventricles

Barkovich, A.J., et al., Normal maturation of the neonatal and infant brain: MR imaging at 1.5 T. Radiology, 1988. 166(1): p. 173-180.

Thank you!