Title. Myelin-Sensitive T1w/T2w Ratio MRI for Deep Learning–Based Infant Developmental Age Estimation

Purpose. To investigate whether the T1w/T2w ratio image (RI)—a myelin-sensitive contrast from routine MRI—improves deep learning–based infant developmental age estimation, whether a biologically informed multi-task model further enhances performance, and whether predictions remain clinically meaningful in myelin-related pathologies.

Materials and Methods. We retrospectively analyzed 629 infants aged 0–24 months from a public pediatric MRI dataset: 626 with age-appropriate myelination for modeling and 3 with myelin-related pathologies (hemorrhage, infarction, atrophy) for qualitative case review. Developmental age was assigned by a pediatric neuroradiologist blinded to chronological age. RI generation involved: 1) linear registration of T2w to T1w 2) brain extraction and bias correction 3) nonlinear registration to an 18-month pediatric template 4) voxel-wise T1w/T2w division. Five inputs (T1w, T2w, T1w+T2w, RI, T1w+T2w+RI) were compared in two 3D CNNs, ResNet18 and ChenNet. The proposed RI-based multi-task model added auxiliary white matter segmentation, RI reconstruction, and multi-scale prediction across four encoder depths. Five-fold cross-validation with two seeds was performed; modality effects used ANOVA with Welch t-tests; Grad-CAM assessed interpretability.

Results. RI achieved the lowest MAE: 1.304±0.176 months (r=0.973) in ResNet18 and 1.306±0.208 (r=0.970) in ChenNet, outperforming T1w (1.694/1.853), T2w (1.531/1.512), T1w+T2w (1.462/1.403), and T1w+T2w+RI (1.356/1.349). ANOVA confirmed modality effects ($p<0.001$); RI outperformed T1w and T2w ($|d|=1.03$-1.83, large), while differences from T1w+T2w+RI were non-significant ($|d|\leq 0.31$, $p\geq 0.49$), indicating RI captured most information. The proposed multi-task model further improved the RI model (MAE 1.203; r=0.979). Grad-CAM localized RI attention to periventricular white matter and the posterior limb of the internal capsule, regions of early myelination. In three held-out cases (hemorrhage, infarction, atrophy), RI or tri-modal predictions matched the adjusted age more closely than T1w+T2w (1mo: 2.0 vs. 3.8; 7mo: 6.7 vs. 8.1; 12mo: 11.8 vs. 14.4); these exploratory findings warrant further validation.

Conclusion. T1w/T2w ratio MRI with deep learning enables accurate developmental age estimation, further improved by auxiliary tasks; case review suggests RI-based predictions may reflect atypical myelination, supporting RI as a myelination-sensitive biomarker from routine MRI.

Clinical Relevance Statement. RI from routine T1w and T2w may provide a quantitative adjunct to visual myelination assessment, supporting objective developmental age estimation without additional MRI acquisition.

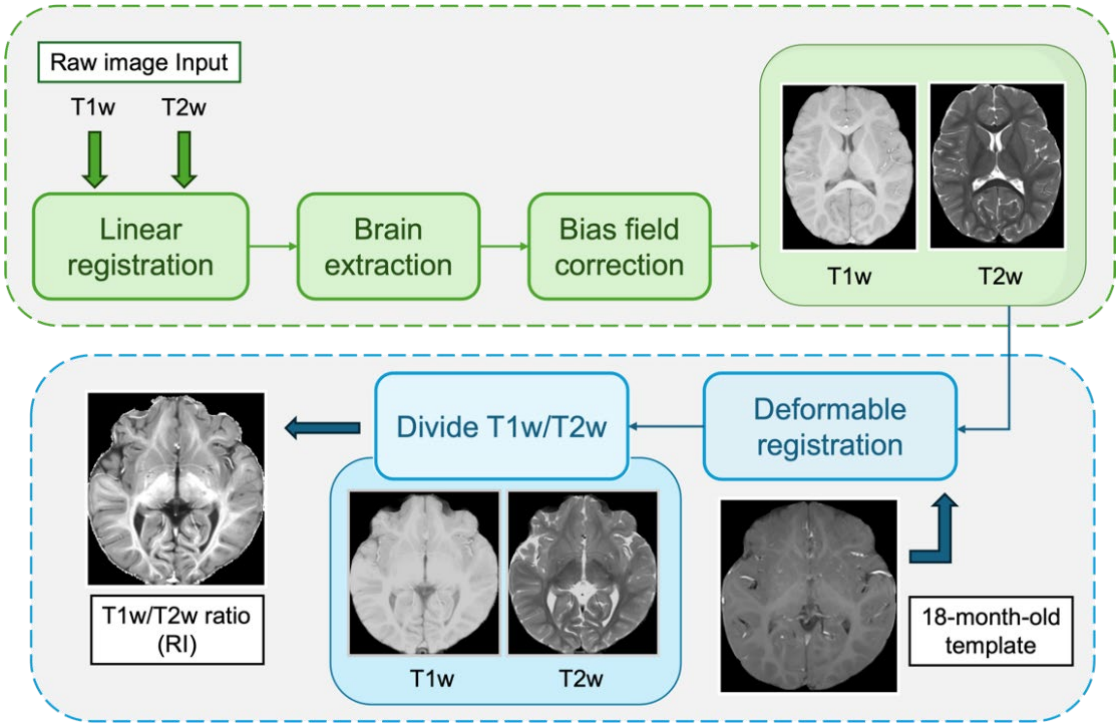


Figure 1. Schematic overview of the T1w/T2w ratio image (RI) generation pipeline. RI is computed through four sequential steps: (1) linear registration of T2w to T1w; (2) brain extraction and bias field correction; (3) nonlinear registration to an 18-month pediatric brain template; (4) voxel-wise division of the preprocessed T1w by T2w. Steps performed in native image space are shaded green; those in template space are shaded blue. The resulting RI provides myelin-sensitive contrast for input to 3D CNN–based developmental age estimation.

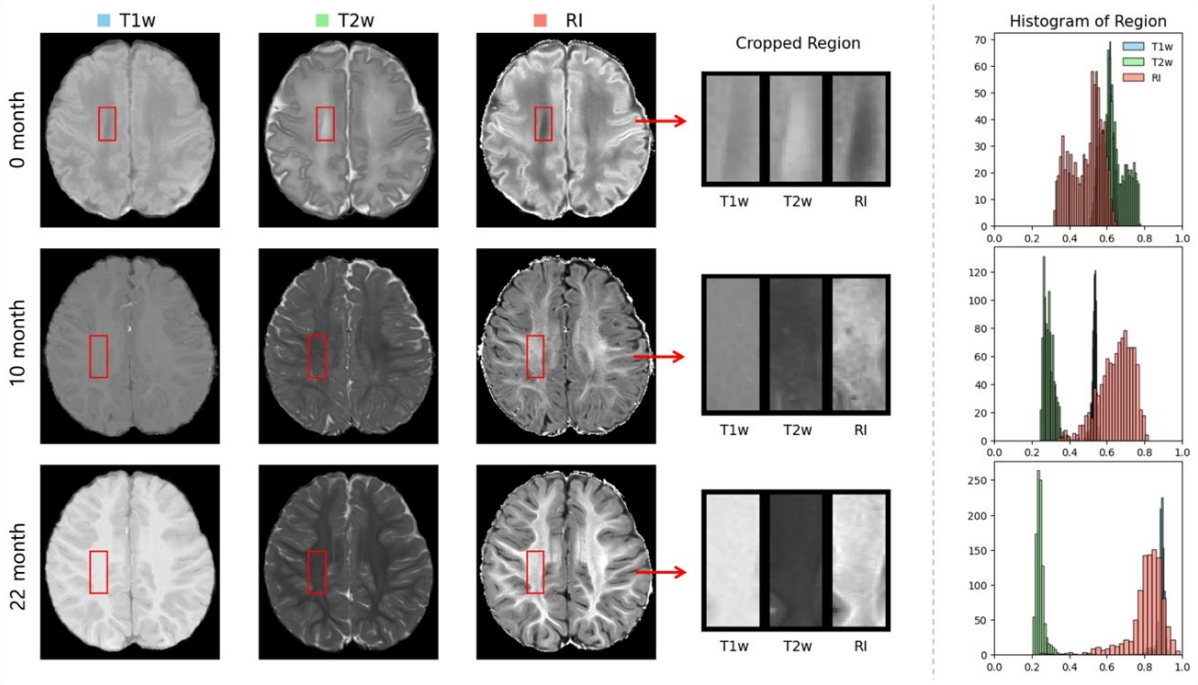


Figure 2. Age-dependent RI contrast evolution. Age-dependent contrast evolution of T1w, T2w, and RI images in infants aged 0, 10, and 22 months, with white matter ROIs (red boxes) and corresponding intensity histograms (right). With increasing age, T1w white matter signal increases and T2w white matter signal decreases, enhancing RI contrast between white and gray matter. RI highlights maturation-related white matter changes and provides biologically meaningful input for developmental age estimation.

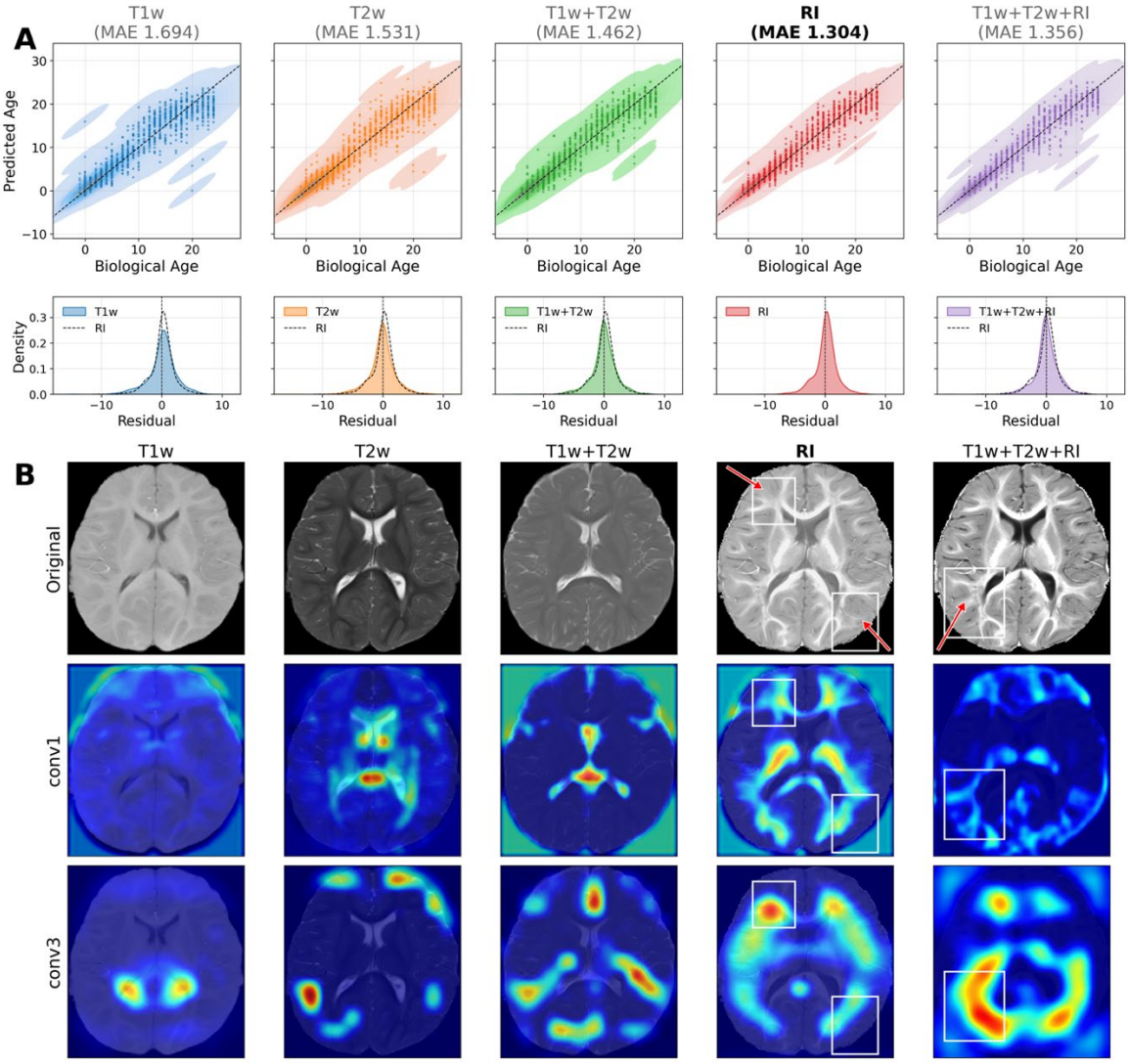
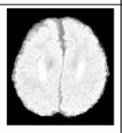
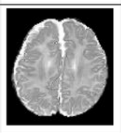
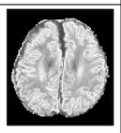
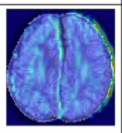
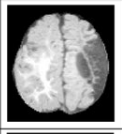
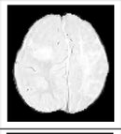
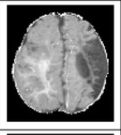
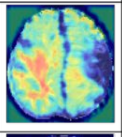
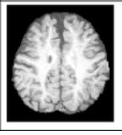
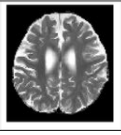
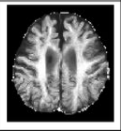
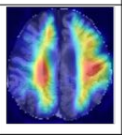


Figure 3. Performance and interpretability across input modalities (ResNet18; similar trends in ChenNet). **(A)** Scatter plots of predicted versus biological age with per-modality MAE (top), and residual distribution overlaid with the RI reference (bottom, dashed); RI shows the tightest alignment and narrowest residuals. **(B)** Grad-CAM at early (conv1) and late (conv3) layers for a representative subject. RI-based models localize attention to periventricular white matter and the posterior limb of the internal capsule (arrows)—regions of early myelination—whereas T1w or T2w alone show diffuse or peripheral attention.

Table 1. Prediction performance (mean±SD across 5-fold cross-validation) for ChenNet, ResNet18 and the proposed multi-task multi-scale RI model across input modalities. Within each baseline model, **bold with underline** marks the best-performing modality and **bold** marks the second-best. The proposed multi-task model, trained with RI input, is listed separately and achieves the overall best performance.

Modality	ChenNet					ResNet18				
	MAE ↓	RMSE ↓	ρ ↑	r ↑	R^2 ↑	MAE ↓	RMSE ↓	ρ ↑	r ↑	R^2 ↑
T1w	1.853 ±0.432	2.622 ±0.557	0.939 ±0.018	0.947 ±0.019	0.883 ±0.046	1.694 ±0.245	2.460 ±0.401	0.948 ±0.016	0.950 ±0.014	0.899 ±0.026
T2w	1.512 ±0.192	2.231 ±0.296	0.958 ±0.006	0.960 ±0.008	0.918 ±0.017	1.531 ±0.212	2.289 ±0.289	0.957 ±0.005	0.958 ±0.009	0.913 ±0.019
T1w+T2w	1.403 ±0.166	2.151 ±0.238	0.960 ±0.005	0.963 ±0.006	0.924 ±0.012	1.462 ±0.222	2.112 ±0.239	0.962 ±0.006	0.966 ±0.006	0.926 ±0.015
RI	**1.306** ±0.208	**1.927** ±0.312	**0.966** ±0.009	**0.970** ±0.009	**0.938** ±0.019	**1.304** ±0.176	**1.842** ±0.246	**0.975** ±0.006	**0.973** ±0.007	**0.944** ±0.013
T1w+T2w+RI	**1.349** ±0.218	**2.032** ±0.300	**0.964** ±0.005	**0.968** ±0.007	**0.932** ±0.015	**1.356** ±0.157	**1.968** ±0.239	**0.967** ±0.005	**0.970** ±0.006	**0.936** ±0.013
Proposed multi-task multi-scale RI model										
RI*	**1.201** ±0.217	**1.701** ±0.342	**0.972** ±0.008	**0.975** ±0.009	**0.950** ±0.020	**1.203** ±0.169	**1.696** ±0.256	**0.975** ±0.006	**0.979** ±0.008	**0.954** ±0.015

Figure 4. Case-level performance in three infants with myelin-related pathologies excluded from model training. Rows: chronological age, radiologist-adjusted developmental age, and diagnosis (left); representative axial T1w, T2w, RI, and RI-based Grad-CAM (middle); predicted age per input with signed error from the adjusted age in parentheses (right). Within each case, **bold** marks the prediction closest to the adjusted age; underline marks the second-closest. In all three cases, RI or tri-modal (T1w+T2w+RI) predictions align most closely with the radiologist-adjusted age. Grad-CAM concentrates in periventricular white matter rather than on the focal lesion, reflecting global myelination rather than focal pathology.

Age	Adj. Age	Diagnosis	T1	T2	RI	G-CAM (RI)	T1	T2	T1+T2	RI	T1+T2 +RI
4	1	Intracerebral hemorrhage					2.2 (+1.2)	2.6 (+1.6)	3.8 (+2.8)	**2.0 (+1.0)**	3.5 (+2.5)
9	7	Premature, Infarct					4.7 (-2.3)	1.9 (-7.1)	8.1 (+1.1)	**6.7 (-0.3)**	5.5 (-1.5)
14	12	Cerebral atrophy					14.5 (+2.5)	14.9 (+2.9)	14.4 (+2.4)	12.6 (+0.6)	**11.8 (-0.2)**