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Feasibility and Clinical Value of Synthetic Magnetic Resonance Imaging to Evaluate Total Brain Maturity of Newborns

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Abstract

Objectives
To verify the feasibility and clinical value of synthetic magnetic resonance imaging (SyMRI) for evaluating total maturation score (TMS) and to explore its correlation with gestational age (GA) in newborns.
Methods
A total of 106 neonates within 28 days of birth were recruited for this study. Each subject underwent MRI examinations, including axial T1- and T2-weighted imaging and SyMRI sequences. TMS was calculated using SyMRI (SyTMS) and conventional T1- and T2-weighted images (cTMS), respectively. The consistency between cTMS and SyTMS was evaluated, along with the parameters of glial cell migration band involution (B score), germinal matrix presence (G score), myelination (M score), and cortical infolding (C score). Analysis of variance was used to compare the mean values of SyTMS in the preterm groups (including preterm cerebral changes group, preterm with normal routine MRI findings group, and preterm cerebral hemorrhage group) and the full-term control group. Subsequently, Pearson correlation analysis was conducted to examine the relationship between SyTMS and GA.
Results
The correlation coefficients of TMS, M, G, B, and C scores between SyTMS and cTMS were 0.96, 0.87, 0.85, 0.91, and 1.00, respectively ($P < 0.01$). Additionally, GA and SyTMS were strongly and positively correlated [r = 0.74; linear regression equation: SyTMS = -5.63 + 0.50 × GA (weeks)].
Conclusions
The SyTMS score in the neonatal period is equivalent to the TMS score obtained using conventional MRI. SyTMS scores of premature infants with normal MRI structures and signals remained lower than those of full-term infants during the neonatal period.

Highlights

1. SyT1WI and SyT2WI can be used for neonatal brain TMS assessment.

2. GA was identified as an independent factor influencing neonatal brain SyTMS, with a strong linear and positive correlation between them.

3. SyTMS scores of premature infants with normal MRI structures and signals remained lower than those of full-term infants during the neonatal period.

Feasibility and Clinical Value of Synthetic Magnetic Resonance Imaging to Evaluate Total Brain Maturity of Newborns

1.Introduction

The total maturity score (TMS) is a common semi-quantitative scoring system based on conventional MRI for assessing brain morphology and development soon after birth[1, 2]. The TMS is determined by

analyzing brain parenchymal morphology and signal changes on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI). It incorporates 4 parameters: myelination (M score), cortical infolding (C score), involution of glial cell migration bands (B score), and the presence of germinal matrix (G score)[1, 3]. The TMS provides an integrated perspective on brain maturity shortly after birth, distinguishing differences among neonates born at different gestational ages (GAs) and across various pathological conditions[4, 5]. Abnormalities in neonatal MRI, especially in the white matter, can predict cognitive and motor development at the age of 2 years[6]. Research shows that white-matter abnormalities diagnosed using MRI during the neonatal period are related to intelligence, language, executive function, and motor skills at preschool age[7].

Recently, synthetic magnetic resonance imaging (SyMRI) has emerged as a valuable tool in pediatric imaging, including in newborns[8, 9]. It can simultaneously acquire quantitative relaxation time maps and generate multiple contrast maps (such as T1WI and T2WI) in a single scan[10–12]. However, it remains unclear whether SyMRI-based T1WI and T2WI (SyT1WI and SyT2WI, respectively), obtained simultaneously in a single scan, can be used to assess neonatal brain maturity. Additionally, no study has yet reported on the differences in total brain maturity between preterm and full-term neonates evaluated by SyT1WI and SyT2WI. Therefore, this study aimed (1) to verify the feasibility and clinical application value of SyT1WI and SyT2WI for evaluating the TMS in newborns, and (2) to determine the correlation between SyTMS and GA.

2.Materials and Methods

2.1Patients

We prospectively enrolled preterm and full-term neonates admitted to the Department of Neonatology (Hidden information), who underwent head MRI examinations between April 1st, 2020, and December 17th, 2023.

Inclusion criteria:

Preterm cerebral hemorrhage (PCH) group: (a) GA < 37 weeks; (b) age at MR examination (GA at MRI) ≤ 28 days; (c) no congenital infection, congenital metabolic diseases, cranial malformations, or other organ injuries; and (d) detection of cerebral hemorrhage on conventional MRI.

Preterm cerebral changes (PCC) group: (a) GA < 37 weeks; (b) GA at MRI ≤ 28 days; (c) no congenital infection, congenital metabolic diseases, cranial malformations, or other organ injuries; and (d) detection of preterm cerebral changes on conventional MRI.

Preterm with normal routine MRI findings (PNRMRI) group: (a) GA < 37 weeks; (b) GA at MRI ≤ 28 days; (c) no congenital infection, congenital metabolic diseases, cranial malformations, or other organ injuries; and (d) no abnormalities on conventional MRI of the brain.

Patients were excluded if they met any of the following 3 criteria: (1) presence of severe complications, including bilirubin encephalopathy, congenital infections, congenital metabolic diseases, craniocerebral malformations, and other organ injuries, (2) age > 28 days at the time of MRI examination, and (3) obvious motion artifacts or partial pixel loss in the SyMRI scans. GA at MRI was calculated as the sum of the GA and the age at the time of MRI examination.

The present prospective study was approved by the local ethics committee (approval number: 2022WJWZCLL-15), and informed consent was obtained from the newborns' guardians before the MRI examination.

It should be noted that there is a partial overlap between the participants or data analyzed in the current study and those in a previous study[13]. This is because both datasets were derived from two subgroups of the same research project. The earlier study aimed to explore the agreement between SyMRI-derived T1 and T2 relaxation times and T1/T2 values on conventional MRI in the neonatal brain as well as to investigate the correlation between SyMRI T1/T2 values and GA. In contrast, the present study aims to assess the consistency between SyTMS and cTMS, and to examine the relationship between SyTMS and GA in the neonatal brain.

2.2MRI examination

All neonates were sedated via an enema of 10% chloral hydrate (0.5 mL/kg) or an intramuscular injection of phenobarbital (10 mg/kg) 30 min before the MRI examination. Hearing protection was applied during the MRI scan. Head MRI scans were obtained using a 3.0-T scanner (SIGNA Architect, GE Healthcare) with a 48-channel head coil. Conventional MRI scans included axial T1WI and T2WI propeller sequences, followed by multi-dynamic multi-echo (MDME) sequences to acquire SyMRI data. The specific MRI acquisition parameters used in this study are shown in Table 1.

Table 1
Magnetic resonance imaging acquisition parameters

Sequence	Axial SyMRI	Axial T2WI propeller	Axial T1WI	Axial T1-FLAIR	Axial DWI	Sagittal T1-FLAIR
Matrix	288 × 288	320 × 320	320 × 224	320 × 224	160 × 160	320 × 224
Field of view (mm^2)	180 × 180	180 × 180	180 × 180	180 × 135	180 × 135	160 × 160
Slice thickness (mm)	4	4	4	4	4	4
Spacing (mm)	0.4	0.4	0.4	0.4	0.4	1.0
TR (ms)	4364.0	4922.0	700	1750.0	4574.0	1750.0
TE (ms)	21.8	100.1	Minimum	24	90.3	24.0
Pixel size (mm^3)	0.6 × 0.6 × 4	0.6 × 0.6 × 4	0.6 × 0.8 × 4	0.6 × 0.8 × 4	1.1 × 0.8 × 4	0.5 × 0.7 × 4
Number of sections	20	20	20	20	20	15
Acquisition time (min)	5:32	1:24	2:31	1:35	1:02	1:51

SyMRI, synthetic magnetic resonance imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; T1-FLAIR, T1-weighted fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging; TR, repetition time; TE, echo time

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2.3 Imaging diagnosis and Assessment of TMS on MRI

Magnetic Resonance Imaging Diagnosis

PCH group: GA < 37 weeks. Hemorrhage signals observed in any area of the brain (including the cerebrum, cerebellum, brainstem, ventricles, and subarachnoid space). The diagnostic criteria for ultra-acute, acute, subacute, and chronic stages of hemorrhage[14] are detailed in Table 1.

PCC group: GA < 37 weeks. The white matter of the paracentral lobule, and frontal and occipital lobes shows low signal on T1WI and high signal on T2WI[15], and a slightly low signal on the T1WI-fluid-attenuated inversion recovery (FLAIR) sequence.

PNRMRI group: GA < 37 weeks. No abnormal signals were observed on conventional T1WI, T2WI, and T1WI-FLAIR sequences.

Full-term group (T): 37 weeks ≤ GA ≤ 42 weeks. No abnormal signals were observed on conventional T1WI, T2WI, and T1WI-FLAIR sequences.

Assessment of TMS on MRI

MDME data were processed using Synthetic MR software (*v*8.0.4, Synthetic MR, Linkoping, Sweden) to generate axial SyT1WI and SyT2WI. The M, C, B, and G scores were calculated using axial SyT1WI and SyT2WI, and conventional T1WI and T2WI sequences, and then, the TMS was determined[1] (Fig. 1 and Fig. 2).

All the imaging diagnoses of the preterm infants and full-term infants were made by junior doctors with imaging qualifications, and were subsequently reviewed and approved by senior doctors in our hospital. The junior doctors had 3–5 years of experience in radiological diagnosis, while the senior doctors had at least 10 years of experience. A total of 12 junior doctors participated in the primary diagnosis, and 8 senior doctors participated in the diagnosis review. Finally, a senior doctor (Yan Dong) reviewed all the diagnoses, conducted a consistency test, and included the data in this study.

2.4Statistical methods

Statistical analysis was performed using IBM SPSS Statistics *v*26.0. A *P*-value of less than 0.05 was considered statistically significant. Intraclass correlation coefficients (ICCs) were used to test the consistency between the TMS calculated from conventional T1WI and T2WI sequences (conventional group) and that derived from SyT1WI and SyT2WI sequences (synthetic group). The statistical evaluation of ICCs was conducted using the two-way mixed model, with single measurement and absolute agreement type.

The normality of variables was tested using the Shapiro-Wilk test. The distribution of GA, GA at MRI, BW, G scores, B scores, and SyTMS was normal or nearly normal. Therefore, differences in the above parameters were tested using the two-independent samples *t*-test. The Apgar scores at the 1st minute, 5th minute, and 10th minute (Apgar 1, Apgar 5, and Apgar 10) and the M and C scores all showed non-normal distributions. Therefore, these parameters were tested using the rank sum test of two independent samples, and the confidence interval of the median differences was estimated using the Hodges-Lehmann estimator. The chi square test was used for categorical variables such as gender, mode of delivery (C-section or vaginal delivery), maternal complications (complications requiring clinical medication during pregnancy and throughout the labor process, such as hypothyroidism, hyperthyroidism, diabetes, hypertension, and fever), and whether resuscitation was required at birth due to asphyxia.

Multiple comparisons of the mean differences in SyTMS scores among the 4 groups were conducted using analysis of variance (F-test). Pairwise comparisons were performed using the Bonferroni analysis. SyTMS showed a linear correlation with the GA and BW scatter plots, and all of these variables were normally distributed quantitative variables. Therefore, Pearson linear correlation analysis (correlation coefficient: r) was adopted to further compare the correlation coefficients of SyTMS with GA and BW.

Single-factor linear regression was used to explore the relationship of SyTMS with the parameter with the highest correlation coefficient. A *P*-value of less than 0.05 indicated statistical significance.

3.Results

3.1Demographic parameters and clinical characteristics

A total of 124 neonates with appropriate weight for GA were initially included, of whom 15 were excluded due to motion artifacts, and 3 were excluded due to partial pixel loss. Thus, ultimately, 106 neonates (50 full-term and 56 preterm infants) were included in this study (Fig. 3). Eleven preterm infants had cerebral hemorrhage, 25 infants had preterm cerebral changes, and 20 preterm infants had normal results on routine conventional MRI. The demographic characteristics of the enrolled patients, including sex, GA, GA at MRI, and BW, are presented in Table 2. The GA at MRI was calculated as the sum of the GA and the age at MRI examination.

Table 2
Demographic parameters and clinical characteristics

	Total (n = 106)
Quantitative variable	
GA (weeks)	36.71 (35.29, 39.46)
GA at MRI (weeks)	37.64 (36.53, 40.14)
BW(kg)	2.70 ± 0.44
Apgar 1	9 (7, 9)
Apgar 5	10 (9, 10)
Apgar 10	10 (10, 10)
Categorical variable	
Sex (female)	36/106 (34%)
Delivery method (C-section)	53/106 (50%)
Maternal comorbidity	72/106 (67.9%)
Resuscitation due to asphyxiation at birth	29/106 (27.4%)

GA, gestation age; MRI, magnetic resonance imaging; Birth weight, BW; Apgar 1, 5, and 10, Apgar scores at 1, 5, and 10 min after birth; C-section, cesarean section

3.2Consistency between SyTMS and cTMS

Consistency analysis of the TMS obtained using conventional and synthetic T1WI and T2WI sequences showed that the correlation coefficients of the total score, and the M, G, B, and C scores were all greater than 0.85 (Table 3). SyT1WI sequences displayed local abnormal small bleeding more clearly than conventional T1WI (Figs. 4 and 5).

Table 3
Consistency test of TMS and its 4 parameters between conventional MRI and synthetic MRI

SyTMS	ICC	95% CI	F-value	*P*-value
	0.96	**(0.93, 0.98)**	**49.09**	**< 0.001**
M score	0.87	(0.77, 0.93)	15.52	< 0.001
G score	0.85	(0.72, 0.92)	12.56	< 0.001
B score	0.91	(0.82, 0.95)	22.00	< 0.001
C score	1.00	(1,1)	-	-

ICC, intraclass correlation coefficient; CI, confidence interval; SyTMS, total maturation score based on synthetic MRI; MRI, magnetic resonance imaging; M score, myelination; G, presence of germinal matrix tissue; B, involution of glial cell migration bands; C, cortical infolding

3.3Correlation analysis of SyTMS scores

The correlation between GA and SyTMS (r = 0.74) was higher than that between BW and SyTMS (r = 0.64). GA was an independent influencing factor for SyTMS (Table 4), and the linear regression equation of GA and SyTMS was as follows: SyTMS = -5.63 + 0.50 × GA (weeks).

Table 4
Univariate linear regression analysis of SyTMS and GA

Variable	B	β	t-value	*P*-value	Adj-R^2	F-value
GA	-0.50	0.74	11.35	< 0.001	0.55	128.92

SyTMS, total maturation score based on synthetic magnetic resonance imaging; GA, gestational age; B, unstandardized regression coefficient; β, standardized regression coefficient; Adj-R^2, adjusted R-squared

3.4 Differences in SyTMS scores among the 3 groups of premature infants and the full-term control group

The SyTMS scores of the full-term group were higher than those of the preterm groups PCH, PCC, and PNRMRI (all P values < 0.001). No statistically significant differences in SyTMS scores were found among the 3 subgroups of preterm infants (*P* > 0.05; Table 5).

Table 5
Difference in SyTMS scores between the preterm infant groups and the full-term infant group

Group	*Group*	*Mean difference and 95% CI*	*P*-value
T	PNRMRI	2.80 (1.96, 3.64)	< 0.001
	PCH	2.37 (1.32, 3.43)	< 0.001
	PCC	2.34 (1.56, 3.12)	< 0.001
PNRMRI	T	-2.80 (-3.64, -1.96)	< 0.001
	PCH	-0.43 (-1.62, 0.76)	1.000
	PCC	-0.46 (-1.41, 0.49)	1.000
PCH	T	-2.37 (-3.43, -1.32)	< 0.001
	PNRMRI	0.43 (-0.76, 1.62)	1.000
	PCC	-0.03 (-1.18, 1.11)	1.000
PCC	T	-2.34 (-3.12, -1.56)	< 0.001
	PNRMRI	0.46 (-0.49, 1.41)	1.000
	PCH	0.03 (-1.11, 1.18)	1.000
Preterm cerebral hemorrhage, PCH			
Preterm cerebral changes, PCC			
Preterm with normal routine MRI findings, PNRMRI			
Term, T			

4.Discussion

4.1Assessment of TMS

Consistency analysis of the TMS scores obtained using conventional and synthetic T1WI and T2WI sequences showed that the correlation coefficients of the total score, and the M, G, B, and C scores were all greater than 0.85, indicating that the TMS and its 4 parameters were highly consistent between conventional MRI and SyMRI. The SyTMS values in preterm and full-term infants were also consistent with the scores obtained using conventional T1WI and T2WI. This is in line with previous reports[16] that the image quality of SyT1WI and SyT2WI is comparable to that of conventional T1WI and T2WI. SyT1WI and SyT2WI sequences can complement or replace conventional T1WI and T2WI sequences, in terms of image quality and diagnostic performance, for the investigation of focal cystic white matter lesions in preterm infants[16].

Among the 4 TMS parameters, cortical infolding was the only parameter that was evaluated using T1WI sequences, and the consistency of C scores between the conventional sequences and synthetic sequences reached 100%, mainly because this score is largely based on fronto-occipital morphology and signal contrast differences between gray and white matter[1]. Image quality and signal contrast differences between gray and white matter are approximately identical on SyT1WI and conventional T1WI[17], and in our study, SyT1WI sequences displayed local abnormal small bleeding more clearly than conventional T1WI (Fig. 4). The other 3 TMS parameters (M, G, and B scores) were assessed on T2WI sequences[1], and the overall image quality of SyT2WI was comparable to that of conventional T2WI, indicating that SyMRI could be used in clinical practice[18]. However, in 2 patients, the M and G parameters were less clear on SyT2WI than on conventional T2WI, and needed to be carefully identified. This may be due to the fact that the contrast-to-noise ratio and image quality of SyT2WI sequences are slightly inferior to those of conventional T2WI[19].

4.2TMS characteristics in newborns

Cortical infolding is a biomarker of gray-matter maturation[20], and studies have shown that the degree of cortical infolding is lower in preterm infants than in full-term infants[4]. Brain myelination is a long process that occurs throughout human life (from the fetal period to 60 years of age)[21]. Myelination is considered normal for the neonatal period when two-thirds of or the complete posterior limb of the internal capsule is displayed (M score, 4 points), and the presence of one-third or less of the tail part (M score, 3 points) indicates delayed myelination[22].

In the newly revised brain maturity score, the G and B scores do not differ between full-term infants and preterm infants at an equivalent age[20]. Under the new criteria, the maximum G and B scores have been reduced from 4 points to 2 points. Under the new criteria, only mature brains have G and B scores of 2 points, while immature brains have G and B scores of 1 point each. The gray and white matter in the brains of full-term infants do not fully mature in the neonatal period[20], and neuronal migration in the frontal lobe does not completely disappear during the neonatal period. Moreover, the germinal matrix can be observed along the top of the temporal horn of the lateral ventricle, over the head of the caudate nucleus, or along the lateral wall of the occipital horn of the lateral ventricle in the neonatal period[23]. Therefore, changing the original G and B parameters from 4 points to 2 points may be insufficient to depict the maturity differences between preterm infants and full-term infants.

Interestingly, in our study, the hospitalization rate of female infants was lower than that of male infants, which may be related to important differences between male and female innate immune responses in preterm and full-term newborns[24].

4.3Correlation analysis of SyTMS

From the linear regression equation SyTMS = 0.50 × GA (weeks) − 5.63 (Table 4), it can be seen that the SyTMS was linearly and positively correlated with GA, which is consistent with previous research that conventional MRI-based TMS is significantly correlated with GA and increases with GA[1]. The slope constant in our study was 0.50, which is similar to the slope constant of 0.65 in the earliest linear

regression study of TMS and GA[1]. In contrast, in another study on TMS and preterm infants at term postmenstrual age[4], the linear regression equation of TMS and postmenstrual age was Y (TMS) = 1.164 × (postmenstrual age) − 28.888, and the slope constant was 1.164. The slope constant of the linear regression equation in the above study is larger than the slope constant in our study and that in the earliest linear regression study of TMS and GA[1]. With an increase in the slope constant, the changes in the TMS will be more significant with increases in GA, and may not truly reflect the changes in maturity with GA.

4.4 Analysis of differences in SyTMS scores between preterm infant groups and the full-term infant control group

Brain parenchymal hemorrhage and periventricular white matter softening diseases in preterm infants with brain injury are closely related to late death and disability in children[25]. Premature infant brain injury or abnormal maturity is a dynamic process[26], and in addition to visible lesions on MRI, there are also microstructural and metabolic abnormalities that evolve over time. Studies have found that some premature infants, despite having no visible brain injury manifestations on conventional MRI, still have impaired maturation processes of neural glial progenitor cells and neurons[27], and longitudinal follow-up has found that some of them develop neurological and motor developmental disorders[25, 28]. For this reason, we included premature infants with normal conventional MRI findings in our study.

We found that the SyTMS scores of the full-term group were higher than those of all the preterm infant groups (PCC, PNRMRI, and PCH), and there were no statistical differences in SyTMS scores among the PCC, PNRMRI, and PCH groups. The lack of significant differences among the SyTMS scores of the 3 preterm groups might be related to the fact that there were not many cases of brain hemorrhage located at the interventricular foramen level (among 11 cases of brain hemorrhage, only 2 cases involved the interventricular foramen level) and to the definition of PCC (visible differences in the contrast of gray and white matter signals in the frontal and occipital lobes[29]). One study has pointed out that bilateral low signal areas in the frontal and occipital lobes may indicate delayed maturation in premature infants, but have no real pathological significance[29].

Interestingly, a statistically significant difference in SyTMS scores was noted betweenPNRMRI group and the full-term group. Quantitative indicators cannot be identified by the naked eye, but can be observed using SyTMS scores. This suggests that in future clinical work, if no bleeding or periventricular white matter softening or other brain injury signs are detected on routine conventional MRI sequences of premature infants, instead of making a diagnosis of “no abnormality on MRI”, clinicians should add SyTMS brain maturity assessment, which may reveal maturation abnormalities in the premature infant brain.

4.5Clinical applications, potential defects, and artifacts of SyMRI

SyMRI is a single-cycle, multi-contrast imaging technique[30]. Conventional MRI brain sequence acquisition takes 20–60 min. SyMRI based on an MDME sequence[31] can obtain quantitative relaxation times covering the entire brain and complete anatomical imaging in just 6 min[10], and multiple contrast images can be obtained within 1 min[11]. Thus, a single scan can produce multiple MRI sequences, such as T1WI, T2WI, T1WI/T2WI–FLAIR. Brain parenchymal volume and intracranial volume obtained using SyMRI can be routinely applied in clinical practice[16, 32]. On the T1WI/T2WI scans generated using SyMRI, differences in myelin formation between full-term and preterm infants can be intuitively and sensitively detected[33].

SyMRI is sensitive to motion artifacts. Researchers have proposed a solution to this potential defect by improving image quality using deep learning. Ryu et al.[34] proposed a deep learning artifact-correction technique based on convolutional neural networks combined with perceptual loss functions. Hagiwara et al.[35] adopted another deep learning approach—a pixel-level neural network based on the loss function of conditional generative adversarial networks—to solve the same problem. Both studies successfully achieved artifact correction while maintaining the contrast of SyMRI FLAIR images. The convolutional neural network model proposed by the former study was also verified in different scanning environments[36].

Another method to improve the quality of SyMRI images is Adaptive Iterative Reconstruction Deep Learning (AIR Recon DL) technology (GE Healthcare), an image-reconstruction method based on deep learning. It is mainly used for the reconstruction of medical images such as MRI and computed tomography images. Its working principle is to build a deep neural network and use a large amount of training data to learn the process of image reconstruction. Specifically, AIR Recon DL automatically adjusts the network parameters by comparing the original image data with high-quality images, thereby achieving gradual optimization and reconstruction of the images. This method can not only improve the signal-to-noise ratio of the image but also reduce the reconstruction time and enhance the image quality[37]. In clinical applications, AIR Recon DL has demonstrated the advantages of effectively reducing imaging time and improving image clarity, providing the possibility of real-time analysis of medical images[38].

4.6Limitations

First, SyMRI scans are very sensitive to motion artifacts, and some signals are lost in MAGiC. Second, a slice thickness of 4 mm for neonatal SyMRI sequences is a bit thick, and currently, regions of interest can only be manually placed on SyMRI scans. Third, the present study did not evaluate the prognosis of preterm and full-term neonates. Our research team is currently investigating the association of neonatal SyTMS with prognostic assessments of preterm infants at 12 months, 24 months, and 36 months.

In summary, SyT1WI and SyT2WI sequences can be used to score brain maturity in neonates born at different GAs. GA was an independent factor influencing neonatal SyTMS, and the 2 were linearly and positively correlated.

5.Conclusions

The SyTMS score in the neonatal period is equivalent to the TMS score obtained using conventional MRI. SyTMS scores of premature infants with normal MRI structures and signals remained lower than those of full-term infants during the neonatal period.

Abbreviations

Abbreviation	Full form
AIR Recon DL	Adaptive Iterative Reconstruction Deep Learning
B score	Bands of migrating glial cells score
C score	Cortical infolding score
cTMS	Total maturation score on conventional MRI
FLAIR	Fluid-attenuated inversion recovery
G score	Germinal matrix score
GA	Gestational age
BW	Birth weight
ICC	Intraclass correlation coefficient
M score	Myelination score
MDME	Multi-dynamic multi-echo
SyMRI	Synthetic magnetic resonance imaging
SyTMS	Total maturation score based on SyMRI
SyT1WI	SyMRI-based T1-weighted imaging
SyT2WI	SyMRI-based T2-weighted imaging
TMS	Total maturation score
T1WI	T1-weighted imaging
T2WI	T2-weighted imaging

Declarations

Author contributions

Investigation, YD and LL; Methodology, ZPZ, YD, XYD, HY, ZWH, GC, WC, YFH, YYT and LL; Resources, ZPZ, YFH, YYT and LL; Software, WC; Supervision, ZPZ; Validation, YD; Writing – original draft, YD and

XYD; Writing – review & editing, ZPZ and LL.

Institutional Review Board Statement

The present prospective study was approved by the local ethics committee (approval number: 2022WJWZCLL-15).

Informed Consent Statement

Informed consent was obtained from all the newborns' guardians involved in the study.

Data Availability Statement

The data is unavailable due to privacy or other reasons.

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Conflicts of Interest

All authors declare that there is no conflict of interest regarding the publication of this paper.

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Figures

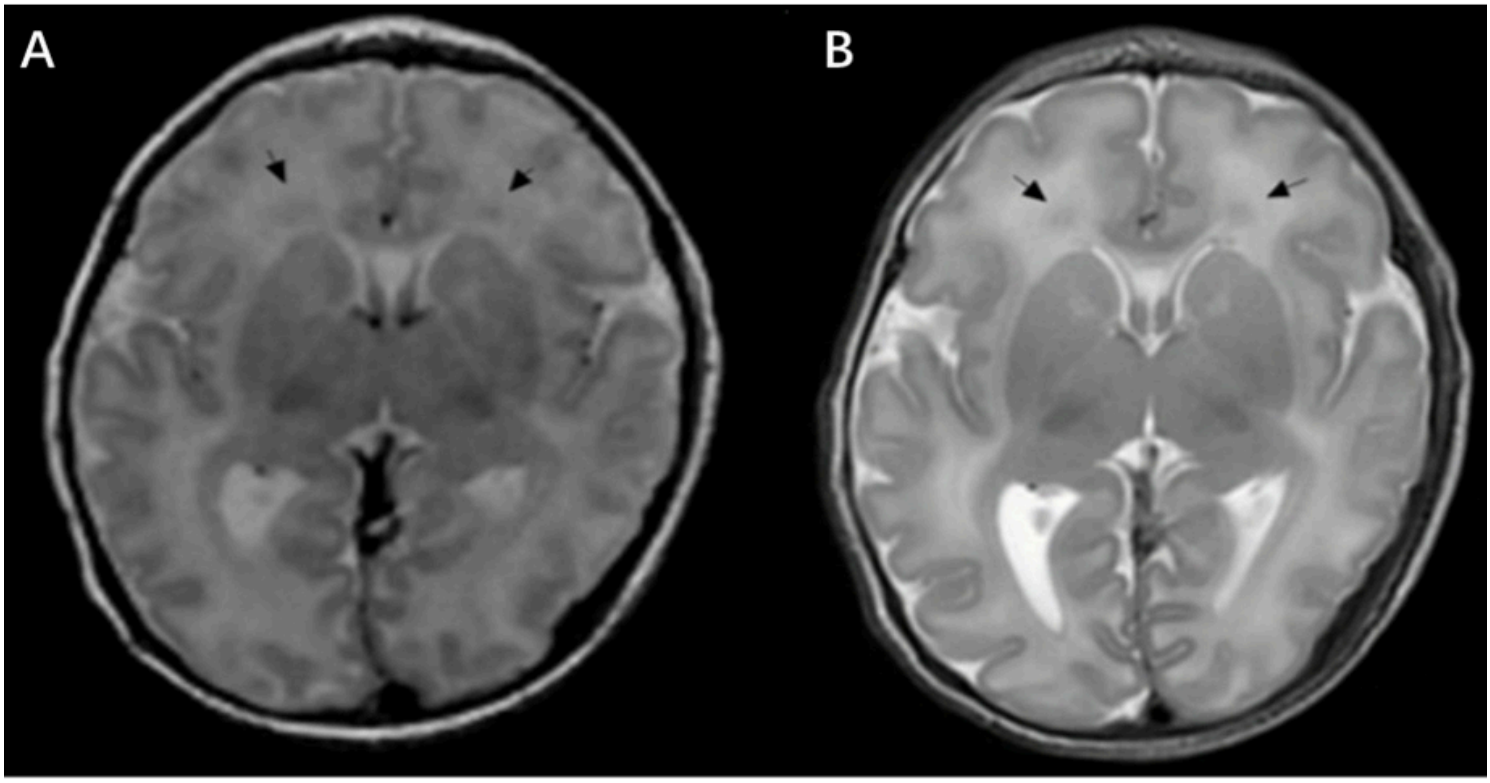


Figure 1

Assessment of involution of glial cell migration bands (B score) onSyT2WI **(A)** and conventional T2WI **(B)**

In a preterm infant with a gestational age of 35 weeks and 2 days, B scores were assessed on SyT2WI and conventional T2WI taken at the level of the basal ganglia level. A wide band and low signal shadow (arrows) are seen in the deep white matter of the frontal lobe around the ventricle. B score = 2.

SyT2WI, T2-weighted imaging based on synthetic magnetic resonance imaging; conventional T2WI, T2-weighted imaging based on conventional magnetic resonance imaging

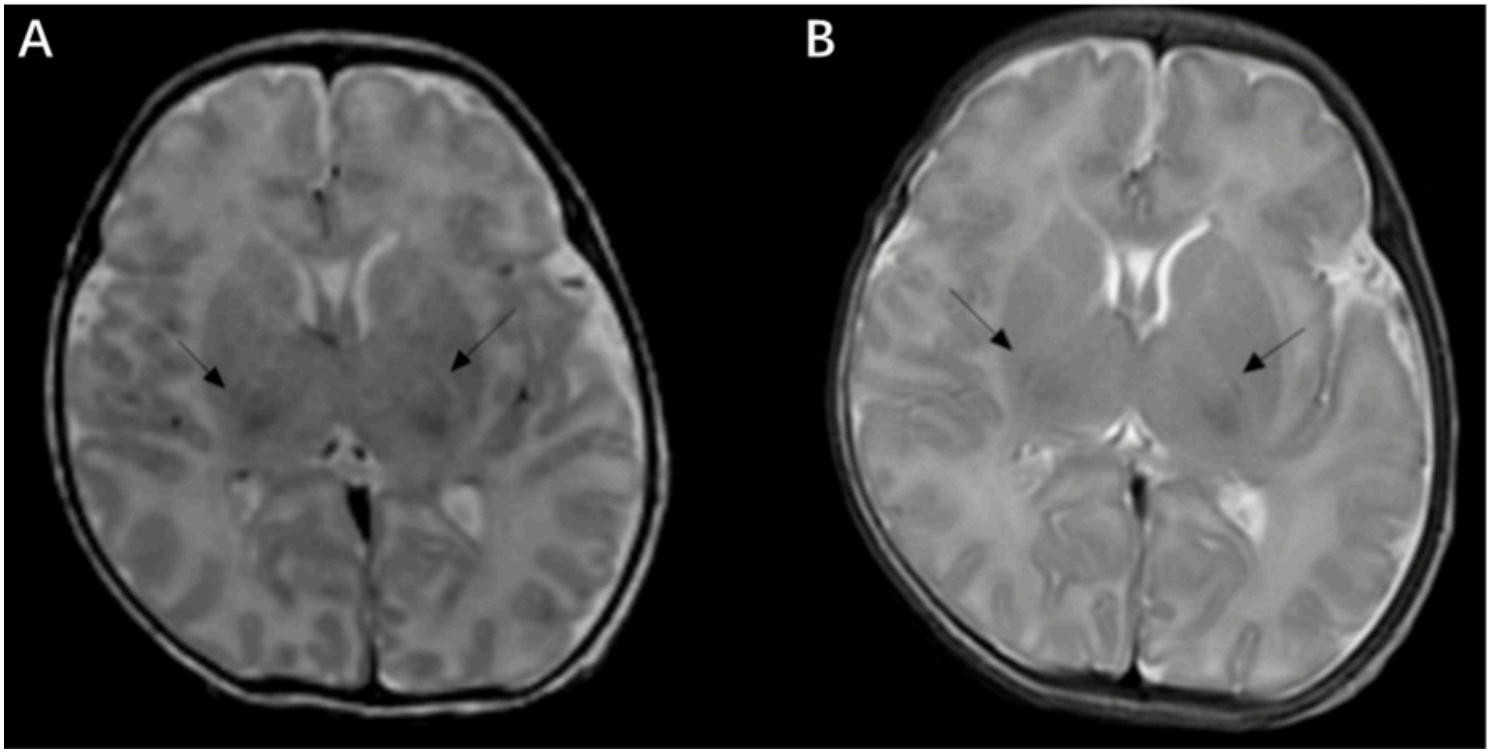


Figure 2

Assessment of myelination (M scores) on **(A)** SyT2WI and **(B)** conventional T2WI

In a preterm infant with a gestational age of 35 weeks and 2 days, M scores were assessed on SyT2WI and conventional T2WI sequences taken at the level of the basal ganglia. The posterior end of the internal capsule is seen (arrows), and the M score is 3. In this case, SyT2WI showed that the caudal side of the posterior limb of the internal capsule needed to be carefully identified.

SyT2WI, T2-weighted imaging based on synthetic magnetic resonance imaging; conventional T2WI, T2-weighted imaging based on conventional magnetic resonance imaging

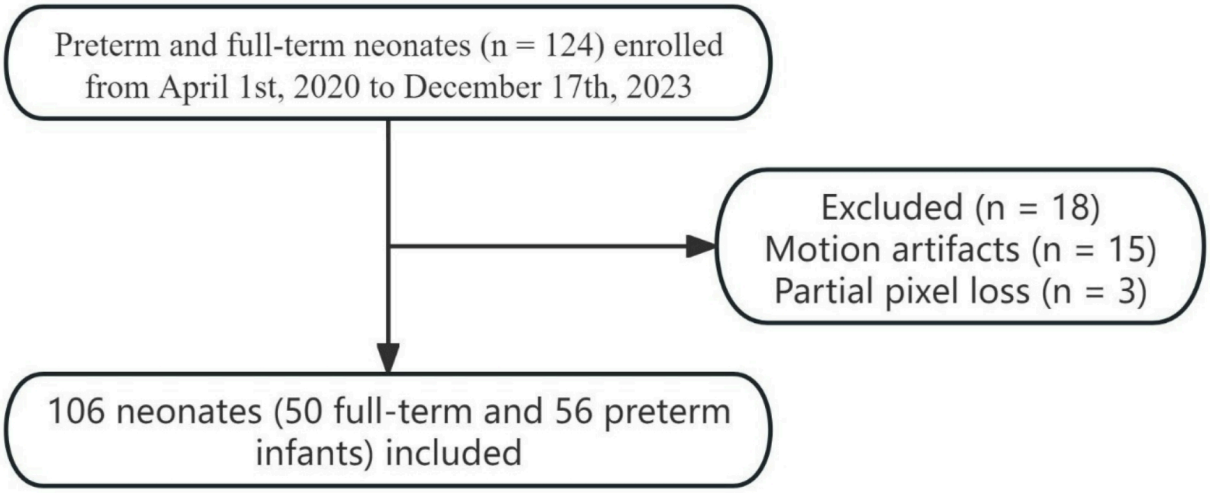


Figure 3

Flowchart of enrollment of preterm and full-term neonates

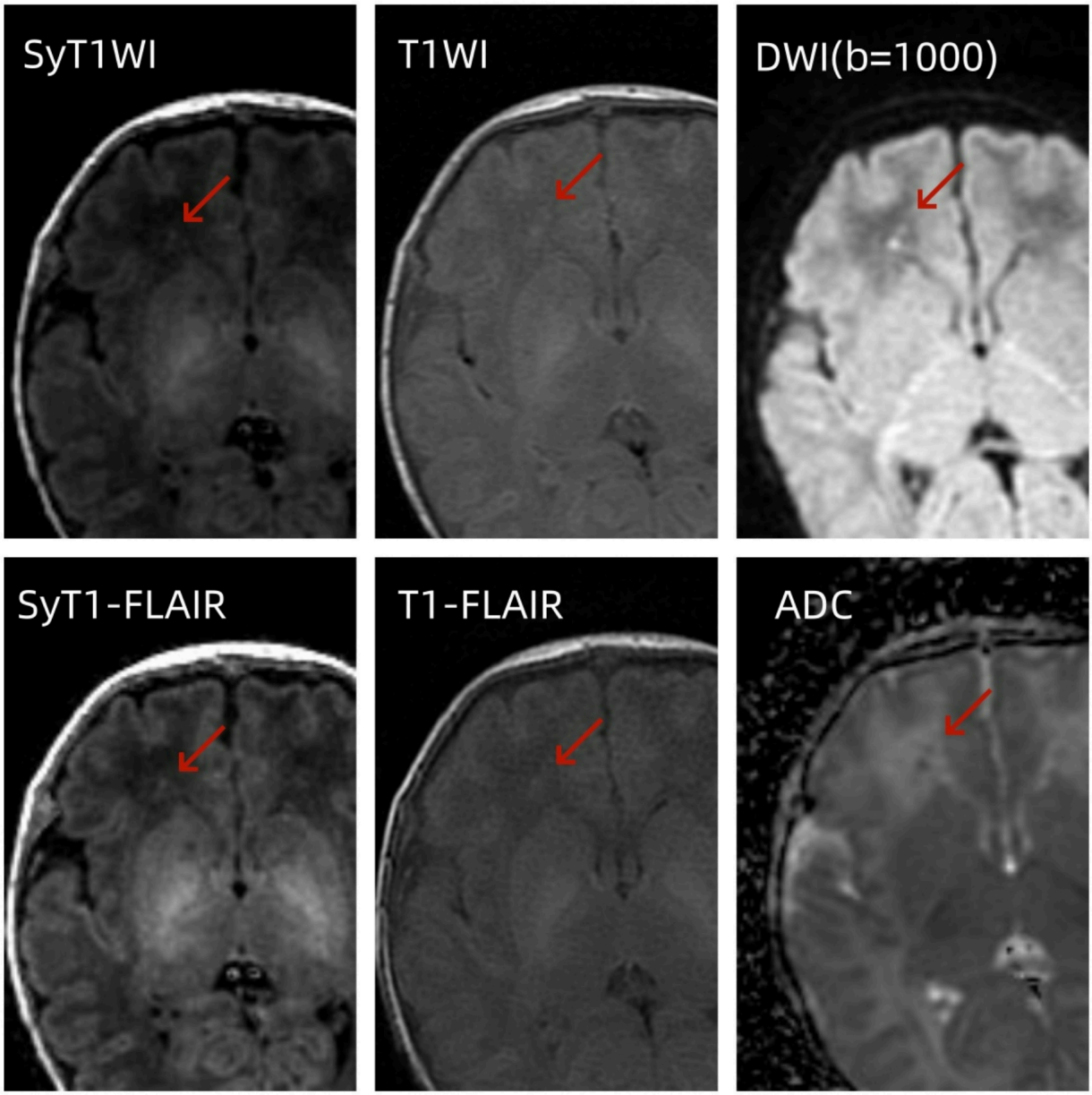


Figure 4

SyT1WI has advantages over conventional T1WI in showing local abnormal small bleeding, which can be seen in the deep white matter in the right frontal lobe beside the anterior horn of the right lateral ventricle (red arrows)

Sy, indicates sequences based on synthetic magnetic resonance imaging.

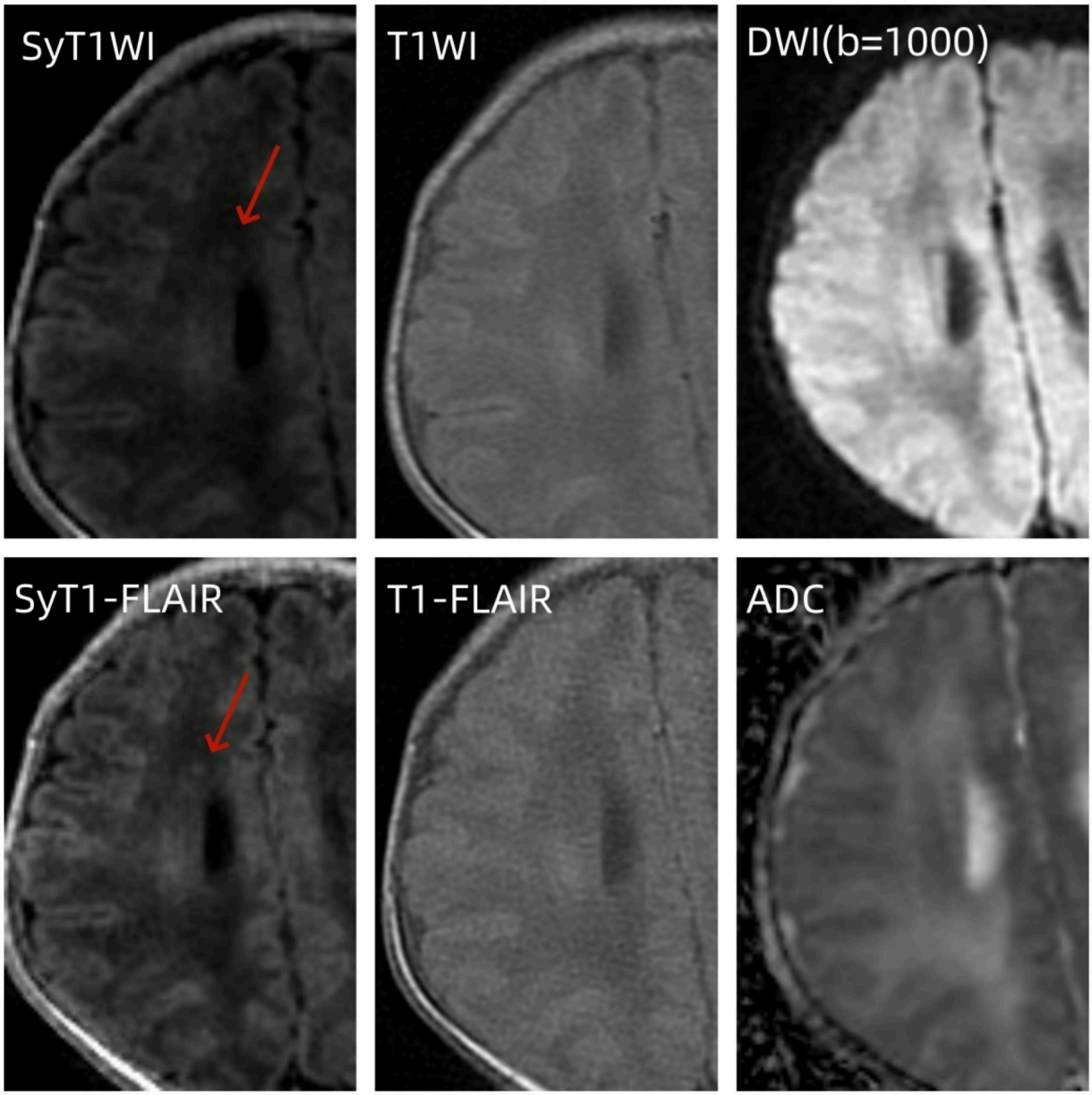


Figure 5

SyT1WI has advantages over conventional T1WI in showing local abnormal small bleeding, which can be seen in the right corona radiata (red arrows)

Sy, indicates sequences based on synthetic magnetic resonance imaging.