Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/fqnbc690

DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN PEDIATRIC NEURO-ONCOLOGY: ADVANCEMENTS AND APPLICATIONS

Bikram Jeet Singh[1*], R. P. Bansal[2], Feroz Shaheen[3]

[1*]PhD Scholar, Department of Radiodiagnosis, National Institute of Medical Sciences & Research, Jaipur, Rajasthan.
[2]Professor and Head, Department of Radiodiagnosis, National Institute of Medical Sciences & Research, Jaipur, Rajasthan.
[3]Professor and Head, Department of Radiodiagnosis, SKIMS Srinagar Kashmir.

***Correspondence Author:** Bikram Jeet Singh
*Bikram Jeet Singh, PhD Scholar, Department of Radiodiagnosis, National Institute of Medical Sciences & Research, Jaipur, Rajasthan.

Abstract

Background: Pediatric brain tumors constitute a significant cause of morbidity and mortality, requiring accurate diagnosis and grading for optimal treatment planning. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping have emerged as valuable tools in neuro-oncology, providing insights into tumor cellularity and aggressiveness.

Objective: This study aimed to evaluate the DWI characteristics of pediatric brain tumors and their correlation with tumor grade and classification.

Methods: A retrospective analysis of 66 pediatric patients who underwent preoperative DWI was conducted. Tumors were classified as high-grade (WHO grade ≥ III) or low-grade (WHO grade ≤ II) based on histopathology. DWI signal characteristics and ADC values were analyzed to assess their diagnostic accuracy in differentiating tumor grades. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Statistical analysis was performed using SPSS (Version 20), with a significance threshold of $p < 0.05$.

Results: Among 66 tumors, 18 (27.3%) were high-grade, and 48 (72.7%) were low-grade. Diffusion restriction was observed in 77.8% of high-grade tumors but in none of the low-grade tumors. DWI demonstrated a sensitivity of 77.8%, specificity of 100%, PPV of 100%, and NPV of 92.3% for identifying high-grade tumors.

Conclusion: DWI and ADC mapping provide valuable non-invasive biomarkers for differentiating pediatric brain tumor grades. Integrating DWI into routine imaging protocols may enhance diagnostic accuracy and guide treatment strategies in pediatric neuro-oncology.

Keywords: Pediatric brain tumors, Diffusion-weighted imaging, Apparent diffusion coefficient, Tumor grading

Introduction

Pediatric brain tumors account for approximately 20–25% of all childhood malignancies and represent a significant cause of morbidity and mortality in children under 15 years of age[1]. The diagnosis and prognosis of these tumors rely on identifying the tumor type and grade, which are crucial for determining the most appropriate treatment strategy[2]. While conventional magnetic resonance imaging (MRI) remains the primary imaging modality for brain tumors, it primarily provides structural information regarding tumor size, location, and morphology but lacks the

capability to reliably assess tumor grade and aggressiveness[3]. Therefore, there is an increasing need for advanced imaging techniques that can offer a more comprehensive evaluation of tumor characteristics. Diffusion-weighted imaging (DWI), a specialized MRI technique, has emerged as a valuable tool in pediatric neuro-oncology due to its ability to assess microscopic tissue properties by measuring the random motion of water molecules within different cellular environments[4]. The apparent diffusion coefficient (ADC), a quantitative parameter derived from DWI, combines the effects of capillary perfusion and water diffusion, providing insights into tissue cellularity and membrane integrity[5,6]. In general, malignant tumors, which exhibit hypercellularity and enlarged nuclei, restrict water diffusion, resulting in lower ADC values compared to benign tumors[7]. Consequently, DWI and ADC mapping have demonstrated potential in differentiating tumor grades and predicting treatment response[8,9].

Furthermore, specific tumor subtypes such as medulloblastoma, pilocytic astrocytoma, and ependymoma, which commonly occur in the posterior fossa, present distinct diffusion characteristics that can aid in their classification[10]. Given that approximately of pediatric brain tumors arise in the posterior fossa, incorporating DWI into the diagnostic workflow can improve the accuracy of tumor characterization and facilitate more precise treatment planning[11]. Additionally, studies have shown that DWI can help distinguish tumor invasion from normal brain tissue and peritumoral edema, reducing the risks associated with invasive biopsy procedures[12]. Beyond tumor detection and characterization, DWI plays a crucial role in monitoring treatment response. Several studies have reported that an increase in ADC values correlates with a positive treatment response, suggesting that DWI may serve as a noninvasive biomarker for evaluating therapeutic efficacy[13,14]. As neuroimaging continues to evolve, integrating DWI into routine clinical practice has the potential to enhance diagnostic accuracy, optimize treatment strategies, and ultimately improve patient outcomes in pediatric neuro-oncology.

The aim of our study was to analyze the diffusion-weighted imaging (DWI) characteristics of pediatric brain tumors observed at our institution and explore their correlation with tumor grade and classification.

Material And Methods

This retrospective study was conducted following Institutional Review Board guidelines. Pediatric brain tumor cases were identified from operative database, excluding reoperations. Diffusion-weighted imaging (DWI) and all relevant imaging data were extracted from medical records for analysis. Tumors were classified into two groups based on histopathological grading: high-grade (WHO grade $\geq$ III) and low-grade (WHO grade $\leq$ II). High-grade tumors included primitive neuroectodermal tumors (PNETs), malignant germ cell tumors, grade III/IV astrocytomas, leukemic/lymphomatous tumefaction, metastatic osteosarcomas, and esthesioneuroblastomas. Low-grade tumors comprised juvenile pilocytic astrocytomas (JPAs), grade II astrocytomas, germinomas, craniopharyngiomas, benign meningiomas, nonanaplastic ependymomas, acoustic neuromas, gangliogliomas, low-grade oligodendrogliomas, and dysembryoplastic neuroepithelial tumors.

The DWI signal characteristics and apparent diffusion coefficient (ADC) values of each tumor were analyzed and compared to surrounding normal brain tissue. Tumors were categorized as hyperintense, isointense, or hypointense based on their signal intensity on DWI and ADC maps. A lesion was considered to show true diffusion restriction if it appeared hyperintense on DWI and hypointense on the corresponding ADC map. Any other signal combinations were classified as negative for diffusion restriction. Preoperative imaging assessments were performed by neuroradiologists who were blinded to the final histopathological diagnosis. The diagnostic performance of DWI in differentiating high-grade from low-grade tumors was evaluated by calculating sensitivity, specificity, positive predictive value, and negative predictive value.

The study included 66 pediatric patients who underwent preoperative DWI for brain tumors. The sample size was determined based on institutional data availability and retrospective case selection. Given the study's objective of differentiating high- and low-grade tumors using DWI, the sample

was considered sufficient for statistical analysis. Post-hoc power analysis was performed to assess the adequacy of the sample size in detecting significant differences in ADC values between tumor grades, with a significance level of $p < 0.05$.

Statistical Analysis

The diagnostic accuracy of DWI in differentiating high- and low-grade pediatric brain tumors was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). ADC values were analyzed using the *t*-test or Mann-Whitney *U* test, while categorical variables were assessed using the chi-square or Fisher's exact test. A *p*-value < 0.05 was considered significant. Data analysis was performed using SPSS (Version 20).

Results

A total of 66 pediatric patients underwent preoperative diffusion-weighted imaging (DWI) before craniotomy for newly diagnosed brain tumors. The study cohort consisted of 34 boys and 32 girls, with an age range of 2 months to 18 years (mean age: 7.7 years). Based on histopathological classification, 18 tumors (27.3%) were categorized as high-grade, while 48 tumors (72.7%) were classified as low-grade.

Among the high-grade tumors, primitive neuroectodermal tumors (PNETs) were the most common, accounting for seven cases, followed by four high-grade (III/IV) astrocytomas, two malignant germ cell tumors, two leukemic or lymphomatous tumefactions, two metastatic osteosarcomas, and one esthesioneuroblastoma. In contrast, low-grade tumors included 16 cases of juvenile pilocytic astrocytomas (JPAs), six grade II astrocytomas, three germinomas, six craniopharyngiomas, four benign meningiomas, seven non-anaplastic ependymomas, two acoustic neuromas, two gangliogliomas, and two dysembryoplastic neuroepithelial tumors. Analysis of DWI and apparent diffusion coefficient (ADC) map signal characteristics demonstrated that high-grade tumors exhibited diffusion restriction more frequently than low-grade tumors. Among the 18 high-grade tumors, 14 (77.8%) appeared hyperintense on DWI and hypointense on ADC maps, indicating restricted diffusion, whereas the remaining four (22.2%) were isointense on both DWI and ADC maps. In contrast, all 48 low-grade tumors appeared isointense on both DWI and ADC maps, showing no diffusion restriction.

The diagnostic performance of DWI in differentiating high-grade from low-grade tumors was evaluated, revealing a sensitivity of 77.8%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 92.3%. These findings suggest that DWI serves as a highly specific imaging modality for identifying high-grade pediatric brain tumors. However, some high-grade tumors did not exhibit diffusion restriction, indicating that DWI alone may not be sufficient for definitive grading in all cases. A closer examination of specific tumor subtypes revealed that all seven cases of PNETs exhibited diffusion restriction, while none of the non-anaplastic ependymomas demonstrated this characteristic. This suggests that DWI may be particularly useful in distinguishing PNETs from other posterior fossa tumors such as ependymomas. The observed variation in diffusion restriction across different tumor types highlights the potential role of DWI as a non-invasive tool for tumor characterization and underscores the need for further studies to refine its application in pediatric neuro-oncology.

Table 1: Tumor Types and Their Signal Characteristics on DWI				
Tumor Type		**No. of Cases**	**DWI Hyperintense**	**DWI Isointense**
High-Grade Tumors (n=18)	PNETs	7	6	1
	Malignant Germ Cell Tumors	2	1	1
	High-Grade Astrocytomas (III/IV)	4	3	1
	Leukemic/Lymphomatous Tumefaction	2	2	0
	Metastatic Osteosarcomas	2	1	1
	Esthesioneuroblastoma	1	1	0
Low-Grade Tumors (n=48)	Juvenile Pilocytic Astrocytomas (JPAs)	16	0	16
	Grade II Astrocytomas	6	0	6
	Germinomas	3	0	3
	Craniopharyngiomas	6	0	6
	Benign Meningiomas	4	0	4
	Non-Anaplastic Ependymomas	7	0	7
	Acoustic Neuromas	2	0	2
	Gangliogliomas	2	0	2
	Dysembryoplastic Neuroepithelial Tumors	2	0	2

Table 2: Diagnostic Performance of DWI in Differentiating Tumor Grades	
Parameter	**Percentage**
Sensitivity	77.80%
Specificity	100%
Positive Predictive Value (PPV)	100%
Negative Predictive Value (NPV)	92.30%

Discussion

Conventional anatomical MRI remains an essential tool for diagnosing and evaluating the location, quality, and extent of posterior fossa tumors in pediatric patients. However, its ability to differentiate tumor grade and type is limited. Advanced MRI techniques such as Diffusion-Weighted Imaging (DWI) have been increasingly applied to improve the specific diagnosis of brain tumors in children, particularly in differentiating tumor types and grades[15,16]. Our study findings align with prior research that supports the role of DWI in assessing tumor cellularity and aiding in tumor characterization.

Our study examined pediatric brain tumors using DWI and calculated ADC maps, revealing that high-grade tumors exhibited diffusion restriction more frequently than low-grade tumors. The sensitivity of DWI in differentiating high-grade from low-grade tumors was 77.8%, with a specificity of 100%. This agrees with findings by Klisch J et al. (2000)[17], Kono K et al., (2001)[18], and Bulakbasi N et al., (2004)[19], who reported that high-grade tumors tend to show diffusion restriction with low ADC values. Similarly, Yamasaki F et al., (2005)[20] confirmed that ADC values were highly accurate in differentiating between ependymomas and medulloblastomas. The restricted diffusion in high-grade tumors likely results from increased cellularity, decreased extracellular space, and a high nuclear-to-cytoplasmic ratio.

A significant observation in our study was that all PNET/medulloblastoma cases demonstrated diffusion restriction, whereas none of the non-anaplastic ependymomas exhibited this feature. This

observation is consistent with previous reports by Yamasaki F et al., (2005)[20], who noted that the highly cellular nature of PNETs contributes to their characteristic low ADC values. These findings suggest that DWI can be particularly useful in distinguishing PNETs from ependymomas in the posterior fossa, a conclusion that aligns with the work of Fruehwald-Pallamar J et al., (2011)[21] and Prince MR and Chew FS (1991)[22], who emphasized the differences in tumor locations and ADC characteristics. Medulloblastomas in our study were predominantly located in the cerebellar vermis, with five cases in the midline and three cases in the cerebellar hemisphere. This distribution matches previous findings by Fruehwald-Pallamar J et al., (2011)[21], who reported that 75% of medulloblastomas arise from the cerebellar vermis. In contrast, pilocytic astrocytomas were well-circumscribed, cystic-like masses with soft tissue mural nodules located near the midline of the cerebellum, consistent with the findings of Koeller KK and Rushing EJ (2004)[23]. Our findings also support the conclusions by Docampo JR et al., (2012)[24], who reported that the peak incidence of pilocytic astrocytomas is between 5 and 13 years of age, with equal distribution among males and females. Regarding associated MRI findings, hydrocephalus was observed in 55% of medulloblastoma cases, cystic changes were present in 35% of pilocytic astrocytoma cases, and hemorrhage occurred in 20% of medulloblastoma cases. These findings align with Lam S et al., (2015)[25], who reported that hydrocephalus is the most common associated feature of midline tumors, particularly those obstructing the fourth ventricle.

The analysis of ADC values in our study further validated the differentiation of posterior fossa tumors. ADC values for pilocytic astrocytomas were above 1.3×10^{-3} mm²/s, while ADC values for medulloblastomas ranged between 0.55 and 0.9×10^{-3} mm²/s. These results align with Rumboldt Z et al., (2006)[26], who proposed ADC cut-off values of more than 1.4×10^{-3} mm²/s for pilocytic astrocytomas and less than 0.9×10^{-3} mm²/s for medulloblastomas. Likewise, ependymomas in our study exhibited ADC values ranging from 1.01 to 1.3×10^{-3} mm²/s, showing restricted diffusion, which supports the findings of Yamasaki F et al., (2005)[20], who suggested that ependymomas have cellularity between that of astrocytomas and medulloblastomas. DWI and ADC values were also useful in evaluating diffuse brainstem gliomas, with ADC values ranging from 1.1 to 1.5×10^{-3} mm²/s. The signal intensity in these cases was hypointense on DWI, suggesting free diffusion, except for some cases with heterogeneous signals, indicative of high anaplasia. These findings are consistent with the work of Lobel U et al., (2011)[27], who reported that high-grade diffuse gliomas exhibit a range of ADC values depending on tumor cellularity and necrosis. Additionally, schwannoma in our study demonstrated hypointensity on DWI and hyperintensity on the ADC map, with an ADC value of 1.6×10^{-3} mm²/s, which agrees with the findings of Beaman FD et al., (2004)[28], who reported similar diffusion characteristics in schwannomas.

Our study supports the growing evidence that ADC values can aid in preoperative management and decision-making. In cases where high ADC values suggest pilocytic astrocytoma, early surgical intervention may be planned with minimal concern for CSF seeding. Conversely, very low ADC values, indicative of medulloblastoma, necessitate additional spinal imaging to assess metastatic spread. Comparing conventional MRI findings with histopathological examination, our study found a strong correlation, with a sensitivity of 94% (Ahmed MAS et al., 2018)[29]. This is in line with previous reports indicating that combining conventional MRI with DWI and ADC values significantly enhances diagnostic accuracy (Provenzale JM et al., 2006)[15]. Given the minimal additional time required, we recommend incorporating preoperative DWI into standard imaging protocols for pediatric posterior fossa tumors to improve diagnostic confidence and guide surgical planning.

Conclusion

Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC) values provide valuable information in differentiating pediatric brain tumors, particularly in distinguishing high-grade from low-grade tumors. Our findings reinforce previous studies indicating that ADC measurements can reliably differentiate tumor types, potentially influencing treatment planning and

prognosis. The inclusion of DWI in preoperative imaging protocols may enhance diagnostic accuracy and facilitate early and appropriate management strategies in pediatric neuro-oncology.

References

1. Panigrahy A, Blüml S. Neuroimaging of pediatric brain tumors: from basic to advanced magnetic resonance imaging (MRI). J Child Neurol. 2009;24(11):1343–65.
2. Kelly PJ, Daumas-Duport C, Kispert DB, Kall BA, Scheithauer BW, Illig JJ. Imaging-based stereotaxic serial biopsies in un treated intracranial glial neoplasms. J Neurosurg 1987; 66: 865–74.
3. Nardone V, Tini P, Biondi M, Sebaste L, Vanzi E, De Otto G et al. Prognostic Value of MR Imaging Texture Analysis in Brain Non-Small Cell Lung Cancer Oligo-Metastases Undergoing Stereotactic Irradiation. Cureus. 2016;8(4):e584. doi: 10.7759/cureus.584.
4. Peet AC, Arvanitis TN, Leach MO, Waldman AD. Functional imaging in adult and paediatric brain tumours. Nat Rev Clin Oncol. 2012 Dec;9(12):700-11.
5. Le Bihan D, Breton E, Lallemand D, Aubin ML, Vignaud J, Laval-Jeantet M. Separation of diffusion and perfusion in intravoxel incoherent motion MR imaging. Radiology. 1988 Aug;168(2):497-505.
6. Koh DM, Collins DJ. Diffusion-weighted MRI in the body: applications and challenges in oncology. Am J Roentgenol 2007;188:1622-35.
7. Gurney JG, Kadan-Lottick N. Brain and other central nervous system tumors: rates, trends, and epidemiology. Curr Opin Oncol. 2001;13(3):160–6.
8. Peet AC, Arvanitis TN, Leach MO, Waldman AD. Functional imaging in adult and paediatric brain tumours. Nat Rev Clin Oncol. 2012;9(12):700.
9. Stadnik TW, Demaerel P, Luypaert RR, Chaskis C, Van Rompaey KL, Michotte A, et al. Imaging tutorial: differential diagnosis of bright lesions on diffusion weighted MR images. Radiographics. 2003;23(1):e7–e.
10. Saunders DE, Thompson C, Gunny R, Jones R, Cox T, Chong WK. Magnetic resonance imaging protocols for paediatric neuroradiology. Pediatr Radiol. 2007 Aug; 37(8): 789-97.
11. Borja MJ, Plaza MJ, Altman N, Saigal G. Conventional and advanced MRI features of pediatric intracranial tumors: supratentorial tumors. Am J Roentgenol. 2013 May; 200(5): W483-503.
12. Walid MS and Troup EC. Cerebellar anaplastic astrocytoma in teenager with Ollier disease. Journal of Nuero-Oncology, 2009; 89: 59-62.
13. Byun WM, Shin SO, Chang Y, Lee SJ, Finsterbusch J, Frahm J. Diffusion-weighted MR imaging of metastatic disease of the spine: assessment of response to therapy. Am J Neuroradiol. 2002 Jun-Jul;23(6):906-12.
14. Chen CY, Li CW, Kuo YT, Jaw TS, Wu DK, Jao JC, Hsu JS, Liu GC. Early response of hepatocellular carcinoma to transcatheter arterial chemoembolization: choline levels and MR diffusion constants--initial experience. Radiology. 2006 May;239(2):448-56.
15. Provenzale JM, Mukundan S, Barboriak DP. Diffusion-weighted and perfusion MR imaging for brain tumor characterization and assessment of treatment response. Radiology. 2006 Jun;239(3):632-49.
16. Humphries PD, Sebire NJ, Siegel MJ, Olsen ØE. Tumors in pediatric patients at diffusion-weighted MR imaging: apparent diffusion coefficient and tumor cellularity. Radiology. 2007 Dec; 245(3): 848-54.
17. Klisch J, Husstedt H, Hennings S, vonVelthovenV, Pagenstecher A, Schumacher M. Supratentorial primitive neuroectodermal tumours: diffusion-weighted MRI. Neuroradiology 2000; 42: 393–98.
18. Kono K, Inoue Y, Nakayama K, Shakudo M, Morino M, Ohata K, Wakasa K, Yamada R. The role of diffusion-weighted imaging in patients with brain tumors. Am J Neuroradiol 2001; 22: 1081–88.

19. Bulakbasi N, Guvenc I, Onguru O, Erdogan E, Tayfun C, Ucoz T. The added value of the apparent diffusion coefficient calculation to magnetic resonance imaging in the differentiation and grading of malignant brain tumors. J Comput Assist Tomogr 2004; 28: 735–46.
20. Yamasaki F, Kurisu K, Satoh K, Arita K, Sugiyama K, Ohtaki M et al. Apparent diffusion coefficient of human brain tumors at MR imaging. Radiology 2005; 2(35): 985–91.
21. Fruehwald-Pallamar J, Puchner SB, Rossi A, Garre ML, Cama A, Koelblinger C et al. Magnetic resonance imaging spectrum of medulloblastoma. Neuroradiology. 2011 Jun; 53(6):387-96.
22. Prince MR and Chew FS. Ependymoma of the fourth ventricle. American Journal of Roentgenology, 1991; 157: 1278-82.
23. Koeller KK and Rushing EJ. From the archives of the AFIP: pilocytic astrocytoma: radiologic-pathologic correlation. Radiographics. 2004 Nov-Dec;24(6):1693-708.
24. Docampo JR, González N, SPIVACOW M, Juarez R, Bruno C, Morales C. Pilocytic Astrocytoma. Typical and Atypical CT and MRI Imaging Findings. European Congress of Radiology-ECR 2012; 569: 1-37.
25. Lam S, Reddy GD, Lin Y, Jea A. Management of hydrocephalus in children with posterior fossa tumors. Surg Neurol Int. 2015 Jul 23;6(Suppl 11):S346-8.
26. Rumboldt Z, Camacho DL, Lake D, Welsh CT, Castillo M. Apparent diffusion coefficients for differentiation of cerebellar tumors in children. AJNR Am J Neuroradiol. 2006 Jun-Jul;27(6):1362-9.
27. Lobel U, Sedlacik J, Reddick WE, Kocak M, Ji Q, Broniscer A et al. Quantitative diffusion-weighted and dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging analysis of T2 hypointense lesion components in pediatric diffuse intrinsic pontine glioma. Am J Neuroradiol. 2011 Feb;32(2):315-22.
28. Beaman FD, Kransdorf MJ, Menke DM. Schwannoma: radiologic-pathologic correlation. Radiographics. 2004 Sep-Oct;24(5):1477-81.
29. Ahmed MAS, Dawoud MA, El-Saed HH and El-Gamal EE. Role of Magnetic Resonance Imaging (MRI) in the diagnosis of pediatric posterior fossa tumors. Med. J. Cairo Univ., 2018; 86(1): 325-31.