

Diagnostic Utility of Diffusion-Weighted Imaging in Distinguishing Common Pediatric Posterior Fossa Tumors: A Single Center Retrospective Study

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What is already known on this topic?

- Central nervous system (CNS) tumors rank as the second most prevalent type among pediatric tumors, with roughly 50-60% of cases occurring in the posterior fossa. The apparent diffusion coefficient (ADC), derived from diffusion-weighted imaging, offers quantitative insights into tissue cellularity and microstructural integrity. Studies in the literature assessing ADC parameters of pediatric posterior fossa tumors have utilized diverse measurement methods and parameters, yielding variable statistical outcomes.

What this study adds on this topic?

- The ADC parameters play a crucial role in distinguishing pediatric posterior fossa tumors, particularly between medulloblastoma and pilocytic astrocytoma. Compatible with previous studies, the three most common pediatric posterior fossa tumors, ranked from lowest to highest based on ADC parameters (mean tumor ADC values, and the ratio of mean tumor ADC value to the mean ADC value of normal cerebellar parenchyma), are medulloblastoma, ependymoma, and pilocytic astrocytoma.

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Received: July 1, 2024

Revision Requested: July 27, 2024

Last Revision Received: September 4, 2024

Accepted: September 8, 2024

Publication Date: November 1, 2024

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ABSTRACT

Objective: Pediatric posterior fossa tumors pose diagnostic challenges due to their diverse histopathological features and variable clinical presentations. Conventional magnetic resonance imaging (MRI) serves as the initial diagnostic tool; however, additional modalities, such as diffusion-weighted imaging (DWI), are essential for refining tumor classification. This retrospective single-center study aimed to evaluate the diagnostic utility of apparent diffusion coefficient (ADC) parameters in distinguishing between the most common pediatric posterior fossa tumors.

Materials and Methods: Fifty-nine patients under the age of 18 (27 females and 32 males) with histopathologically diagnosed primary posterior fossa tumors underwent pre-treatment conventional and diffusion MRI. Apparent diffusion coefficient values were measured from solid tumor regions and normal cerebellar parenchyma, with subsequent calculation of tumor/normal cerebellar ADC ratios.

Results: The median ADC values for pilocytic astrocytomas (PAs) were $1786.2 \times 10^{-6} \text{ mm}^2/\text{s}$, ependymomas $1144.9 \times 10^{-6} \text{ mm}^2/\text{s}$, and for medulloblastomas $666.1 \times 10^{-6} \text{ mm}^2/\text{s}$ were significantly different ($P < .001$ for all three). Similarly, the median ADC ratios demonstrated discriminatory potential, with PAs showing the highest ratio (2.46), followed by ependymomas (1.55) and medulloblastomas (0.89) ($P < .001$ for all three). Receiver operating characteristic analysis revealed distinct ADC cutoffs and ratios for differentiating all tumor types from each other.

Conclusion: Despite limitations, such as a small cohort size and different MRI protocols, our results show that ADC metrics are especially useful for distinguishing between the most common pediatric posterior fossa tumors. We recommend that future studies integrate advanced imaging techniques and larger cohorts to improve diagnostic accuracy.

Keywords: Pilocytic astrocytoma, ependymoma, medulloblastoma, child, infratentorial neoplasms, Diffusion magnetic resonance imaging

INTRODUCTION

Tumors affecting the central nervous system (CNS) are a significant cause of morbidity and mortality and rank as the second most common group of neoplasms in childhood. Roughly 50%-60% of these tumors occur in the infratentorial region. Among them, pilocytic astrocytomas (PAs), ependymomas, medulloblastomas, and atypical teratoid rhabdoid tumors (ATRTs) are the most frequently encountered pathologies.¹⁻⁶ However, the diagnosis of pediatric posterior fossa tumors presents substantial challenges due to their diverse histopathological

Cite this article as: Pehlivan UA, Aktekin EH, Yalcin C, Hasbay B, Gunesli A, Alkan O. Diagnostic utility of diffusion-weighted imaging in distinguishing common pediatric posterior fossa tumors: A single center retrospective study. *Turk Arch Pediater.* 2024;59(6):560-566.

features and variable clinical presentations. Accurate differentiation of these tumors is crucial for prognostic prediction.

Conventional magnetic resonance imaging (MRI) is a crucial diagnostic tool for the initial evaluation of pediatric posterior fossa tumors. It allows the tumor location and size, presence of hemorrhage or cystic necrotic changes, and mass effect on surrounding structures to be identified. However, due to the complex nature of pediatric posterior fossa tumors, additional diagnostic methods are often required to improve classification and achieve an accurate diagnosis.^{3,7}

Diffusion-weighted imaging (DWI) has emerged as a pivotal MRI technique for assessing the diffusion of water molecules within tissues. By utilizing apparent diffusion coefficient (ADC) mapping derived from DWI, specialists can obtain quantitative insights into tissue cellularity and microstructural integrity.⁸ Apparent diffusion coefficient values are higher in areas with increased water movement in the interstitium, whereas lower ADC values indicate restricted diffusion due to higher cellularity or more compact tissue structures.⁶ Over the past two decades, interest has grown in the use of ADC values as biomarkers to characterize various intracranial pathologies, including pediatric posterior fossa tumors. The unique histopathological features of these tumors, such as cell density and extracellular matrix composition, profoundly influence their diffusion characteristics, highlighting the potential of ADC mapping as a valuable adjunctive tool for diagnostic assessment.¹⁻⁵ However, there are variations in methodologies for measuring regions of interest (ROI) in previous studies. Apparent diffusion coefficient values and cutoffs with variable specificity and sensitivity have been recorded to distinguish different tumor types.

Given the variability in existing data and limited available information, there is a particular need to focus on this subject. This study aimed to share institutional insights into the diagnostic utility of ADC parameters in pediatric posterior fossa tumors.

MATERIALS AND METHODS

Ethical Considerations, Consent, and Permissions

This retrospective, single-center methodological study was conducted in compliance with the principles of the Declaration of Helsinki. All legal guardians provided written informed consent. This study was approved by the Baskent University Clinical Research Ethics Committee (approval number: KA 24/236, approval date: June 12, 2024).

Patient Selection

This study included patients aged <18 years with confirmed primary posterior fossa tumors who underwent conventional brain and diffusion MRI before treatment between January 2010 and March 2024. The exclusion criteria included patients who had any intervention prior to MRI ($n = 6$), as well as those who experienced technical difficulties in measuring tumor ADC values ($n = 15$). Additionally, four patients (three with gangliogliomas and one with an ATRT) were excluded due to potential negative impacts on the statistical analysis.

Imaging Acquisition

All patients were scanned using a 20-channel head-neck coil on either a MAGNETOM Skyra 3T or MAGNETOM Avanto Fit

1.5T MRI scanner (Siemens Healthineers, Erlangen, Germany). Conventional brain MRI included the following pre- and post-contrast images. Before the intravenous contrast injection, axial and sagittal T1-weighted spin-echo images and T2-weighted spin-echo images and FLAIR sequences were obtained. Diffusion-weighted images were acquired using single-shot spin-echo echo-planar imaging with diffusion sensitivities (b -values) of 0 and 1000 s/mm^2 in three orthogonal directions (Z, Y, and X). Diffusion-weighted image parameters included the following: time to repeat (TR) = 6110 ms, time to echo (TE) = 62 ms, slice thickness = 4 mm, and field of view (FOV) = 220 × 220 mm for 3T and TR = 2750 ms, TE = 64 ms, slice thickness = 4 mm, and FOV = 230 × 230 mm for 1.5T. Following intravenous gadolinium-based contrast administration, 3D T1-weighted gradient echo and axial fat-suppressed T1-weighted spin echo sequences were obtained.

Post-Processing and Image Analysis

ADC maps were generated on a pixel-by-pixel basis using standard software (SyngoVia, Siemens Healthineers, Erlangen, Germany). Both the conventional MRI sequences and ADC maps were evaluated by the neuroradiologist who was blinded to the clinical and pathological data. Freehand ROI measurements were performed from the solid tumor components, excluding possible cystic, necrotic, hemorrhagic, and calcified areas (Figure 1). Additionally, the mean ADC value for each patient was calculated using a 1 cm^2 ROI located in the normal cerebellar parenchyma that was unaffected by the tumor or peritumoral areas. All ROI delineations were performed using SyngoVia. The ratio of the mean tumor ADC values to the mean normal cerebellar parenchyma ADC values was also calculated.

Pathological Assessment

Pediatric posterior fossa tumors were classified according to the fifth edition of the World Health Organization (WHO) Classification of CNS Tumors based on initial pathological reports;¹⁴ Pilocytic astrocytomas were categorized as Grade 1 circumscribed astrocytic gliomas. Ependymomas were classified as ependymomas not otherwise specified (NOS) (Grade 2-3) due to molecular testing for specific subtypes being unavailable at our institution. Molecular subtyping (WNT, SHH, and TP53) was not performed for some medulloblastomas; therefore, medulloblastomas were categorized as histopathologically defined medulloblastoma Grade 4.

Statistical Analyses

The primary endpoint of this retrospective study was to assess the feasibility of differentiating pediatric posterior fossa tumors based on pretreatment tumor ADC values. The secondary endpoint included evaluating the relationship between the tumor/normal cerebellar parenchyma ADC ratio and tumor distinguishability. The normality of distribution for continuous variables was confirmed with the Kolmogorov-Smirnov test. Categorical variables were expressed as frequency and percentages, whereas continuous variables were summarized as median and minimum-maximum. The Chi-square test was used to compare categorical variables between the groups. For non-normally distributed data, the Kruskal-Wallis test was used to compare more than two groups. The Bonferroni-adjusted Mann-Whitney U test was used for multiple comparisons of

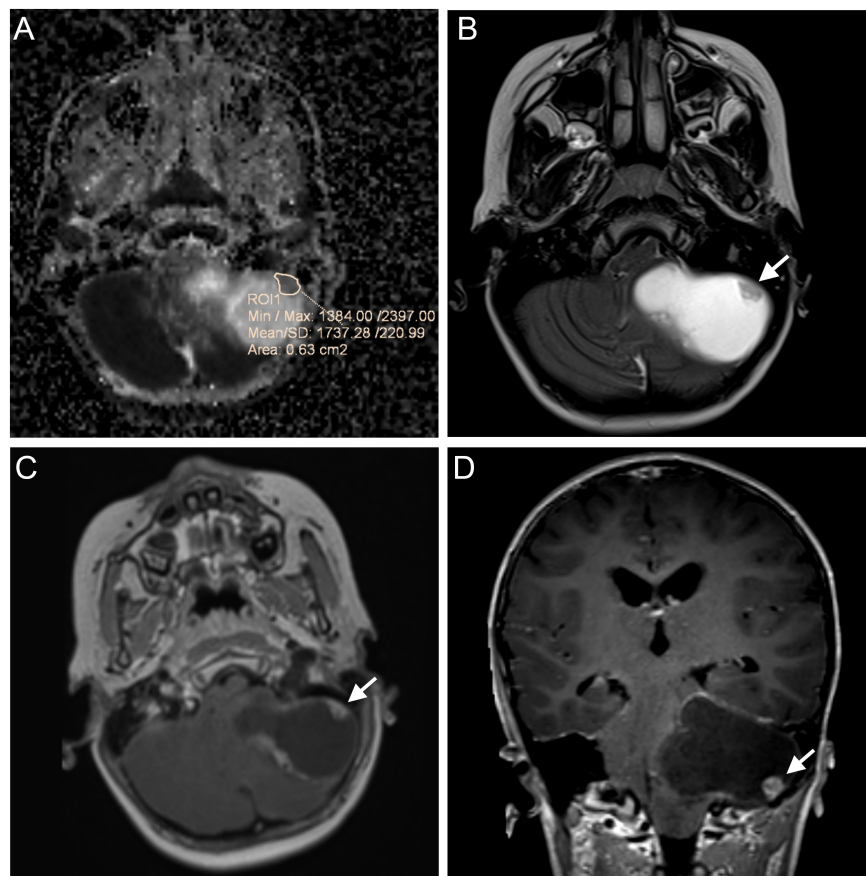


Figure 1. Delineation of the apparent diffusion coefficient measurement (a) in a case of pilocytic astrocytoma with a pronounced cystic component and nodular component, as indicated by the arrow on the T2-weighted image (b). The nodular component exhibits enhancement on post-contrast axial (arrow in c) and coronal (arrow in d) T1-weighted images.

groups. A receiver operating characteristic (ROC) curve analysis was performed in order to identify the optimal cutoff point of ADC parameters. The statistical level of significance for all tests was considered to be .05.

RESULTS

Demographic and Clinical Characteristics

The clinical and pathological characteristics of 59 patients, comprising 27 female individuals (45.76%) and 32 male individuals (54.24%), are summarized in Table 1. The median age of the patients at baseline MRI was 83 (14-210) months for all patients, 71 (29-210) months for PAs, 49 (14-182) months for

ependymomas, and 90 (28-207) months for medulloblastomas. The predominant histopathological diagnoses in this cohort were medulloblastomas (52.54%), followed by PAs (28.81%) and ependymomas-NOS (18.65%). Tumor groups did not differ significantly with respect to sex and age parameters ($P = .409$ and $P = .326$, respectively.).

Distinguishing Pilocytic Astrocytoma, Ependymoma, and Medulloblastoma Using ADC Parameters

The median tumor ADC values were measured as follows: PAs, $1786.2 \times 10^{-6} \text{ mm}^2/\text{s}$ ($1178.0 \times 10^{-6} \text{ mm}^2/\text{s}$ – $3128.6 \times 10^{-6} \text{ mm}^2/\text{s}$); ependymomas-NOS, $1144.9 \times 10^{-6} \text{ mm}^2/\text{s}$ ($796.0 \times 10^{-6} \text{ mm}^2/\text{s}$ – $1578.9 \times 10^{-6} \text{ mm}^2/\text{s}$); and medulloblastomas, $666.1 \times 10^{-6} \text{ mm}^2/\text{s}$

Table 1. Clinical, Radiological and Pathological Characteristics

Characteristics	All Patients (n = 59)	Medulloblastoma (n = 31)	Ependymoma NOS (n = 11)	Pilocytic astrocytoma (n = 17)	P value
Age, months	83 (14-210)	90 (28-207)	49 (14-182)	71 (29-210)	.326*
Sex					
Female (%)	27 (45.76)	12 (38.71)	5 (45.45)	10 (58.82)	
Male (%)	32 (54.24)	19 (61.29)	6 (54.55)	7 (41.18)	.409**
ADC value ($\times 10^{-6} \text{ mm}^2/\text{s}$)	876.8 (443.0-3128.6)	666.1 (443.0-1157.4) ^{¥, €}	1144.9 (796.0-1578.9)	1786.2 (1178.0-3128.6)	<.001*
ADC ratio	1.10 (0.59-4.07)	0.89 (0.59-1.59) ^{¥, €}	1.55 (0.96-2.17)	2.46 (1.63-4.07)	<.001*

NOS: Not otherwise specified, ADC: Apparent diffusion coefficient; ADC ratio: Mean ADC value of tumor/Mean ADC value of the normal cerebellar parenchyma. Unless otherwise specified, data were expressed as median (min-max). *Kruskal-Wallis test was used to compare more than two groups. **Chi-square test was used to compare categorical variables between the groups. [¥] $P < .05$ comparison with Ependymoma NOS. [€] $P < .05$ comparison with Pilocytic astrocytoma.

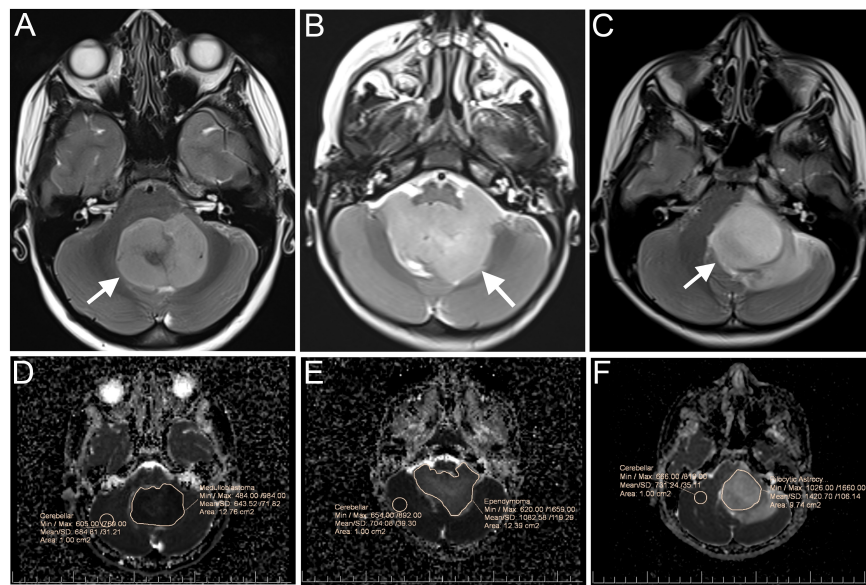


Figure 2. T2 weighted images of medulloblastoma (arrow in a), ependymoma (arrow in b), and pilocytic astrocytoma (arrow in c) are shown. Measurements of apparent diffusion coefficient (ADC) values for normal cerebellar parenchyma and the tumors—medulloblastoma (d), ependymoma (e), and pilocytic astrocytoma (f)—are presented on ADC maps.

$10^{-6} \text{ mm}^2/\text{s}$ ($443.0 \times 10^{-6} \text{ mm}^2/\text{s}$ – $1157.4 \times 10^{-6} \text{ mm}^2/\text{s}$) (Table 1, Figure 2). The ADC values were statistically significantly different among tumor groups, with medulloblastoma exhibiting lower ADC values compared to other groups (Figure 3). According to ROC analysis results, PAs could be distinguished from ependymomas-NOS with 94.1% sensitivity and 90.9% specificity using an ADC value of $\geq 1335.9 \times 10^{-6} \text{ mm}^2/\text{s}$ (area under the curve [AUC]: 95.7%; Youden index: 0.85). Pilocytic astrocytomas could be differentiated from medulloblastomas with 100% sensitivity and specificity using an ADC value of $\geq 1167.7 \times 10^{-6} \text{ mm}^2/\text{s}$ (AUC: 100%; Youden index: 1.0). Ependymomas-NOS could be distinguished from medulloblastomas with 90.9% sensitivity and 90.3% specificity using an ADC value of $\geq 866.5 \times 10^{-6} \text{ mm}^2/\text{s}$ (AUC: 95.9; Youden index: 0.812) ($P < .001$ for each) (Figure 4).

The ADC ratios obtained by dividing the mean ADC values of the tumor by those of the normal cerebellar parenchyma were 2.46 (1.63–4.07) for PAs, 1.55 (0.96–2.17) for ependymomas-NOS, and 0.89 (0.59–1.59) for medulloblastomas. The ADC ratio differed significantly among tumor groups, with medulloblastomas showing lower ADC ratios compared to the other tumor types (Figure 3). According to ROC analysis results, PAs could be distinguished from ependymomas-NOS with 82.4% sensitivity and 81.8% specificity using an ADC ratio of ≥ 1.92 (AUC: 94.7%; Youden index: 0.642). PAs could be differentiated from medulloblastomas with 100% sensitivity and specificity using an ADC ratio of ≥ 1.61 (AUC: 100%; Youden index: 1.0). Ependymomas-NOS could be distinguished from medulloblastomas with 81.8% sensitivity and 80.6% specificity using an ADC ratio of ≥ 1.07 (AUC: 93.3%; Youden index: 0.624) ($P < .001$ for each) (Figure 5).

Additionally, among the 59 patients, 10 underwent imaging with a 3T MRI scanner, while the remaining patients were assessed using a 1.5T MRI scanner. Of the 10 patients assessed with the

3T MRI, five were diagnosed with medulloblastoma, three with PA, and two with ependymoma. A comparison of tumor ADC values and ADC ratios between the two MRI scanners revealed no statistically significant differences ($P = .572$ and $P = .731$, respectively).

DISCUSSION

The main goal of this study was to assess whether ADC parameters obtained from preoperative DWI could distinguish the most commonly observed pediatric tumors of the posterior fossa. Our findings demonstrated significant differences in ADC parameters among medulloblastomas, ependymomas, and PAs, with values decreasing from PAs to medulloblastomas ($P < .001$ for each comparison).

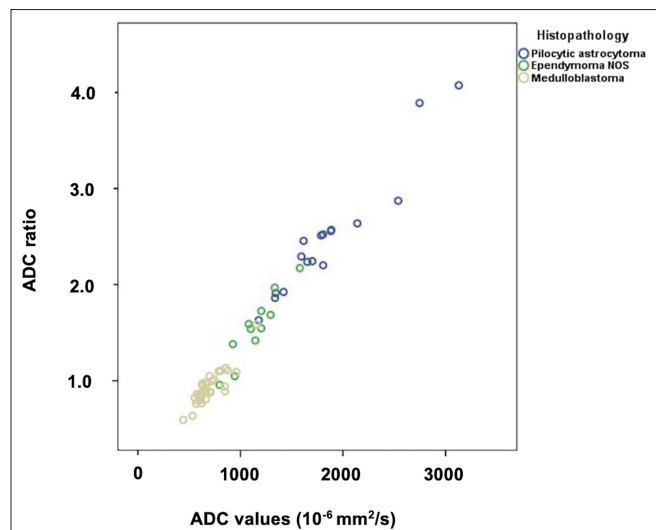


Figure 3. Scatter plot showing the distribution of apparent diffusion coefficient parameters across different tumor groups.

Apparent diffusion coefficient values derived from DWI serve as radiological indicators of tumor cellularity and microstructure.⁸ Over the past two decades, the diagnostic potential of ADC values, combined with conventional MRI, before treatment or intervention has been recognized in pediatric posterior fossa tumors. Additionally, the ratio of tumor ADC values to those of the normal cerebral-cerebellar parenchyma or thalamus has shown promise in enhancing diagnostic accuracy. However, variability in outcomes across these parameters has been previously reported.¹⁻⁴

Rumboldt et al¹ described that mean ADC values for medulloblastomas, ependymomas, and PAs were $660 \pm 150 \times 10^{-6}$ mm²/s, $1100 \pm 110 \times 10^{-6}$ mm²/s, $1650 \pm 270 \times 10^{-6}$ mm²/s, respectively. The authors stated that PAs and medulloblastomas can be distinguished from other pediatric posterior fossa tumors in their cohort by having ADC values of $>1400 \times 10^{-6}$ mm²/s and $<900 \times 10^{-6}$ mm²/s, respectively.¹ In a study by Gimi et al,² two reviewers measured the ADC values of pediatric posterior fossa tumors. Reviewer 1 recorded mean ADC values for ATRTs, medulloblastomas, ependymomas, and PAs of 606.95×10^{-6} mm²/s, 677.67×10^{-6} mm²/s, 1042.11×10^{-6} mm²/s, and 1632.22×10^{-6} mm²/s, respectively. Reviewer 2 reported mean ADC values of 584.62×10^{-6} mm²/s, 687.84×10^{-6} mm²/s, 1008.78×10^{-6} mm²/s, and 1631.41×10^{-6} mm²/s, respectively. The study found a positive correlation between interobserver ADC measurements. The authors also described that ependymomas and medulloblastomas were differentiated with 79% sensitivity and 93% specificity based on an ADC cutoff value of 909×10^{-6} mm²/s; PAs and ependymomas were distinguished with 94% sensitivity and 86% specificity using an ADC threshold of 1250×10^{-6} mm²/s.² Rodriguez Gutierrez et al¹⁵ described

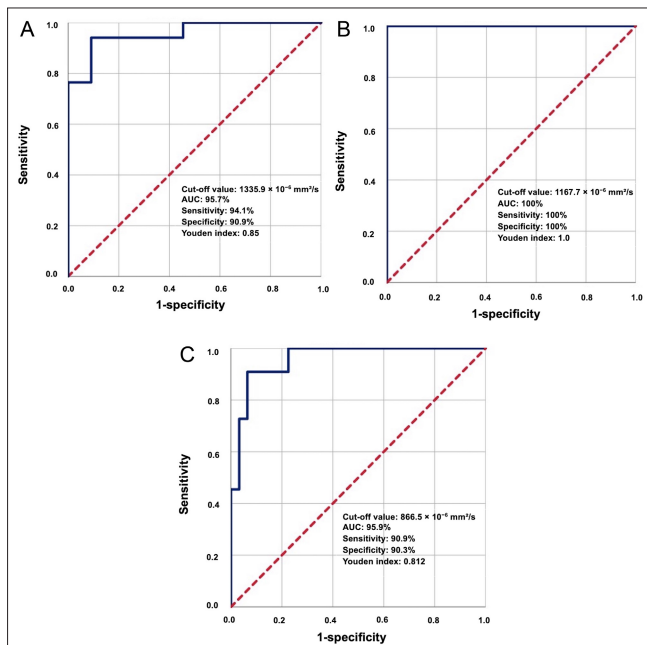


Figure 4. Results of the receiver operating characteristic curve analysis to distinguish pilocytic astrocytoma-ependymoma (a) [area under the curve (AUC): 95.7%; sensitivity: 94.1%, and specificity: 90.9%; Youden index: 0.85], pilocytic astrocytoma-medulloblastoma (b) (AUC: 100%; sensitivity: 100%, and specificity: 100%; Youden index: 1.0), and ependymoma-medulloblastoma (c) (AUC: 95.9%; sensitivity: 90.9%, and specificity: 90.3%; Youden index: 0.812) by tumor apparent diffusion coefficient values before treatment.

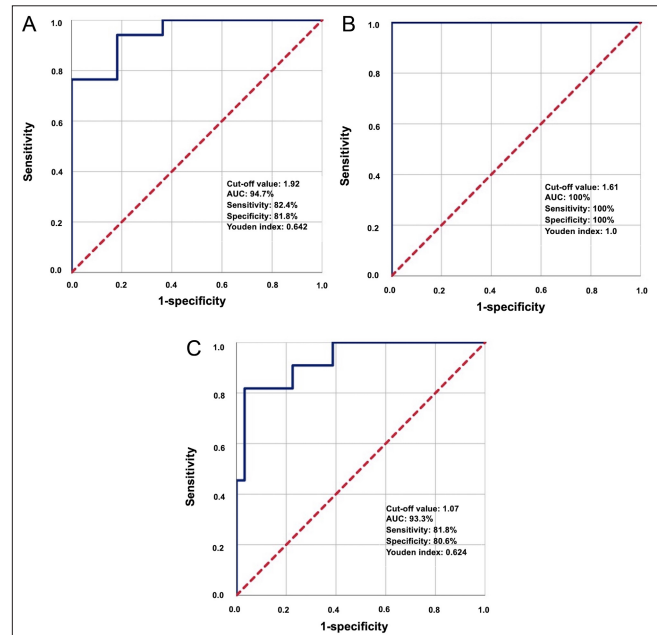


Figure 5. Results of the receiver operating characteristic curve analysis to distinguish pilocytic astrocytoma-ependymoma (a) [area under the curve (AUC): 94.7%; sensitivity: 82.4%, and specificity: 81.8%; Youden index: 0.642], pilocytic astrocytoma-medulloblastoma (b) (AUC: 100%; sensitivity: 100%, and specificity: 100%; Youden index: 1.0), and ependymoma-medulloblastoma (c) (AUC: 93.3%; sensitivity: 81.8%, and specificity: 80.6%; Youden index: 0.624) by the ratio of tumor to normal cerebellar apparent diffusion coefficient values before treatment.

the mean ADC values as $850 \pm 180 \times 10^{-6}$ mm²/s for medulloblastomas, $1340 \pm 290 \times 10^{-6}$ mm²/s for ependymomas, and $1700 \pm 260 \times 10^{-6}$ mm²/s for PAs. Another study reported mean ADC values of medulloblastomas, ependymomas, and PAs of $707.16 \pm 213.47 \times 10^{-6}$ mm²/s, $1035 \pm 217.07 \times 10^{-6}$ mm²/s, and $1427.5 \pm 274.62 \times 10^{-6}$ mm²/s, respectively.³ Novak et al¹⁶ found that the mean ADC values for medulloblastomas, ependymomas, and PAs were $870 \pm 154 \times 10^{-6}$ mm²/s, $1126 \pm 155 \times 10^{-6}$ mm²/s, and $1656 \pm 290 \times 10^{-6}$ mm²/s, respectively. These studies showed that the mean ADC values of the most common pediatric posterior fossa tumors were similar and useful for distinguishing between medulloblastomas, ependymomas, and PAs. Similar to the literature, our study found that the mean ADC values of these tumors were significantly different. The data from the literature and the results from this study are summarized in Table 2. This outcome can be explained by differences in tumor composition. Pilocytic astrocytomas consist of low-density cells, and Rosenthal fibrils have higher ADC values because their extracellular space is wider and their cellularity is lower than those of medulloblastomas and ependymomas.¹⁷ Medulloblastomas, which contain a high nucleus/cytoplasm ratio and, therefore, have tightly packed cells and fewer extracellular regions, show lower ADC values.¹⁸ However, ependymomas have intermediate intense cellularity between medulloblastomas and PAs.^{3,9,10} Koral et al¹⁰ presented a study comparing cellular density and ADC metrics in common pediatric posterior fossa tumors. When these variables were evaluated together with those of ATRTs, medulloblastomas, ependymomas, and PAs, a negative relationship was found between the mean and minimum tumor ADC values and cell densities in common pediatric posterior

Table 2. Summary of Tumor Apparent Diffusion Coefficient Values in the Literature and in Present Study

	Atypical Teratoid Rhabdoid Tumor	Medulloblastoma	Ependymoma	Pilocytic Astrocytoma
Rumboldt et al ¹¹	Not available	660 × 10 ⁻⁶ mm ² /s	1100 × 10 ⁻⁶ mm ² /s	1650 × 10 ⁻⁶ mm ² /s
Gimi et al ^{2*} (Reviewer 1)	606.95 × 10 ⁻⁶ mm ² /s	677.67 × 10 ⁻⁶ mm ² /s	1042.11 × 10 ⁻⁶ mm ² /s	1632.22 × 10 ⁻⁶ mm ² /s
Gimi et al ^{2*} (Reviewer 2)	584.62 × 10 ⁻⁶ mm ² /s	687.84 × 10 ⁻⁶ mm ² /s	1008.78 × 10 ⁻⁶ mm ² /s	1631.41 × 10 ⁻⁶ mm ² /s
Rodriguez Gutierrez et al ^{15*}	Not available	850 × 10 ⁻⁶ mm ² /s	1340 × 10 ⁻⁶ mm ² /s	1700 × 10 ⁻⁶ mm ² /s
Zitouni et al ^{3*}	Not available	707.16 × 10 ⁻⁶ mm ² /s	1035 × 10 ⁻⁶ mm ² /s	1427.5 × 10 ⁻⁶ mm ² /s
Novak et al ^{16*}	Not available	870 × 10 ⁻⁶ mm ² /s,	1126 × 10 ⁻⁶ mm ² /s	1656 × 10 ⁻⁶ mm ² /s
Present study**	Not available	666.1 × 10 ⁻⁶ mm ² /s	1144.9 × 10 ⁻⁶ mm ² /s	1786.2 × 10 ⁻⁶ mm ² /s

*Apparent diffusion coefficient values were expressed as mean. **Apparent diffusion coefficient values were expressed as the median.

Table 3. Comparative Summary of Apparent Diffusion Coefficient Ratios from the Literature and Present Study

	Pilocytic Astrocytoma Versus Ependymoma	Pilocytic Astrocytoma Versus Medulloblastoma	Ependymoma Versus Medulloblastoma
Gimi et al ²	Cut-off ADC ratio: 1.7 Sensitivity: 92% Specificity: 79%	Not available	Cut-off ADC ratio: 1.2 Sensitivity: 93% Specificity: 88%
Koral et al ¹³	Cut-off ADC ratio: 1.8 Sensitivity: 82% Specificity: 76%	Not available	Cut-off ADC ratio: 1.2* Sensitivity: 90% Specificity: 86%
Zitouni et al ³	Cut-off ADC ratio: 1.7 Sensitivity: 85.7% Specificity: 90%	Not available	Cut-off ADC ratio: 1.18 Sensitivity: 100% Specificity: 88.89%
Warinthorn Phuttharak et al ¹¹	Not available	Cut-off ADC ratio: 1.17 Sensitivity: 95.8% Specificity: 100%	Cut-off ADC ratio: 0.995 Sensitivity: 79.2% Specificity: 81.8%
Present study	Cut-off ADC ratio: 1.92 Sensitivity: 82.4% Specificity: 81.8%	Cut-off ADC ratio: 1.61 Sensitivity: 100% Specificity: 100%	Cut-off ADC ratio: 1.07 Sensitivity: 81.8% Specificity: 80.6%

ADC: Apparent diffusion coefficient. *A comparison was conducted between ependymomas and embryonal tumors.

fossa tumors.¹⁰ Although these outcomes support the findings of our study and most of the literature, Koral et al¹⁰ note that tumor cellularity may not be the only determinant of differences in diffusivity. Therefore, with further comprehensive studies on radiological and pathological cooperation, the explanation of other possible causes should be the subject of future research.

Gimi et al² reported that PAs and ependymomas were differentiated with 92% sensitivity and 79% specificity, based on an ADC ratio of >1.7. Moreover, ependymomas and medulloblastomas were distinguishable with 93% sensitivity and 88% specificity using an ADC ratio of >1.2.² Koral et al¹³ documented a retrospective study involving 140 patients from two centers, including 68 with embryonal tumors (58 medulloblastomas, 10 ATRTs), 51 with PAs, and 21 with ependymomas. They reported that PAs and ependymomas were discriminated with 82% sensitivity and 76% specificity using an ADC ratio of ≥1.8. Additionally, ependymomas and embryonal tumors were distinguished with 90% sensitivity and 86% specificity, using an ADC ratio of <1.2. They also highlighted age as a factor, with children aged ≥2 years likely to have medulloblastomas compared with ATRTs for embryonal tumors.¹³ Zitouni et al³ identified that PAs and ependymomas were discriminated with 85.7% sensitivity and 90% specificity based on an ADC ratio

of ≥1.7, while ependymomas and medulloblastomas were differentiated with 100% sensitivity and 88.89% specificity using an ADC ratio of ≥1.18. Warinthorn Phuttharak et al¹¹ described that medulloblastomas were distinguished from other posterior fossa tumors with 95.8% sensitivity and 81% specificity based on an ADC ratio of ≤1.115. They also found that medulloblastomas and ependymomas were differentiated with 79.2% sensitivity and 81.8% specificity using an ADC ratio of ≤0.995. While medulloblastomas were differentiated from PAs with 95.8% sensitivity and 100% specificity based on an ADC ratio of ≤1.17, medulloblastomas and ATRTs were discriminated with 66.7% sensitivity and 50% specificity according to an ADC ratio of ≤0.935.¹¹ Consistent with the results of previous literature, our findings show that medulloblastomas and PAs can be distinguished with high sensitivity and specificity, while discrimination between ependymomas and medulloblastomas and between PAs and ependymomas is relatively more difficult due to overlap. The outcomes of this study and those from the literature are presented in Table 3. This condition may be secondary to ADC changes caused by the local and inflammatory effects of tumors on the microenvironment. Further studies are needed to address these issues.

This study has some limitations. First, this was a single-center, retrospective study with a relatively small cohort. Secondly,

although no statistically significant differences were found between the data obtained from the two different MRI scanners in the current study, images from scanners with different magnetic field strengths and imaging parameters may potentially affect the homogeneity of the data analysis. Third, as observed in other studies in this field, there remains a need to develop new methods to better differentiate overlapping cases, such as distinguishing between PAs-ependymomas, ependymomas-medulloblastomas, and medulloblastomas-ATRTs. Future research involving artificial intelligence and ADC histogram analyses, integrating conventional MRI and DWI, may offer greater clarity regarding these challenging diagnostic distinctions. Moreover, the exclusion of rare cerebellar tumors from our analysis may have slightly affected the sensitivity and specificity of the defined ADC parameters. Additionally, similar to several previous studies, our histopathological analyses lacked molecular staining, precluding a separate investigation of ADC values for medulloblastoma and ependymoma subtypes according to the WHO Classification of CNS Tumors (5th edition). Future studies incorporating molecular data and larger cohorts are essential to obtain more comprehensive insights.

In conclusion, despite these limitations, our study demonstrated that common pediatric cerebellar tumors, particularly those distinguishing between PAs and medulloblastomas, can be identified with high sensitivity and specificity using tumor ADC values and tumor/normal cerebellar ADC ratios. We advocate DWI as the primary tool for evaluating pediatric posterior fossa tumors.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Baskent University (approval no.: 24/236, date: 12 June 2024).

Informed Consent: Written informed consent was obtained from the patients' legal guardians who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – U.A.P., E.H.A., C.Y., B.H.; Design – U.A.P., E.H.A., B.H.; Supervision – A.G., O.A.; Materials – U.A.P., E.H.A., C.Y.; Data Collection and/or Processing – U.A.P., E.H.A., C.Y., A.G., O.A.; Analysis and/or Interpretation – U.A.P., C.Y., B.H., A.G.; Literature Search – U.A.P., E.H.A., B.H., O.A.; Writing – U.A.P.; Critical Reviews – A.G., O.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study received no funding.

REFERENCES

- 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;27(6):1362-1369.
- Gimi B, Cederberg K, Derinkuyu B, et al. Utility of apparent diffusion coefficient ratios in distinguishing common pediatric cerebellar tumors. *Acad Radiol*. 2012;19(7):794-800. [\[CrossRef\]](#)
- Zitouni S, Koc G, Doganay S, et al. Apparent diffusion coefficient in differentiation of pediatric posterior fossa tumors. *Jpn J Radiol*. 2017;35(8):448-453. [\[CrossRef\]](#)
- Jaremko JL, Jans LB, Coleman LT, Ditchfield MR. Value and limitations of diffusion-weighted imaging in grading and diagnosis of pediatric posterior fossa tumors. *AJNR Am J Neuroradiol*. 2010;31(9):1613-1616. [\[CrossRef\]](#)
- Sathyakumar K, Mani S, Pathak GH, Prabhu K, Chacko AG, Chacko G. Neuroimaging of pediatric infratentorial tumors and the value of diffusion-weighted imaging (DWI) in determining tumor grade. *Acta Radiol*. 2021;62(4):533-540. [\[CrossRef\]](#)
- Luo Y, Zhang S, Tan W, Lin G, Zhuang Y, Zeng H. The diagnostic efficiency of quantitative diffusion weighted imaging in differentiating medulloblastoma from posterior fossa tumors: a systematic review and meta-analysis. *Diagnostics (Basel)*. 2022;12(11):2796. [\[CrossRef\]](#)
- Panigrahy A, Blüml S. Neuroimaging of pediatric brain tumors: from basic to advanced magnetic resonance imaging (MRI). *J Child Neurol*. 2009;24(11):1343-1365. [\[CrossRef\]](#)
- Rowley HA, Grant PE, Roberts TP. Diffusion MR imaging. Theory and applications. *Neuroimaging Clin N Am*. 1999;9(2):343-361.
- Gauvain KM, McKinstry RC, Mukherjee P, et al. Evaluating pediatric brain tumor cellularity with diffusion-tensor imaging. *AJR Am J Roentgenol*. 2001;177(2):449-454. [\[CrossRef\]](#)
- Koral K, Mathis D, Gimi B, et al. Common pediatric cerebellar tumors: correlation between cell densities and apparent diffusion coefficient metrics. *Radiology*. 2013;268(2):532-537. [\[CrossRef\]](#)
- Phuttharak W, Wannasarnmetha M, Wara-Asawapati S, Yuthawong S. Diffusion MRI in evaluation of pediatric posterior fossa tumors. *Asian Pac J Cancer Prev*. 2021;22(4):1129-1136. [\[CrossRef\]](#)
- Esa MMM, Mashaly EM, El-Sawaf YF, Dawoud MM. Diagnostic accuracy of apparent diffusion coefficient ratio in distinguishing common pediatric CNS posterior fossa tumors. *Egypt J Radiol Nucl Med*. 2020;51(1):76. [\[CrossRef\]](#)
- Koral K, Alford R, Choudhury N, et al. Applicability of apparent diffusion coefficient ratios in preoperative diagnosis of common pediatric cerebellar tumors across two institutions. *Neuroradiology*. 2014;56(9):781-788. [\[CrossRef\]](#)
- Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the central nervous system: a summary. *Neuro Oncol*. 2021;23(8):1231-1251. [\[CrossRef\]](#)
- Rodriguez Gutierrez D, Awwad A, Meijer L, et al. Metrics and textural features of MRI diffusion to improve classification of pediatric posterior fossa tumors. *AJNR Am J Neuroradiol*. 2014;35(5):1009-1015. [\[CrossRef\]](#)
- Novak J, Zarinabad N, Rose H, et al. Classification of paediatric brain tumours by diffusion weighted imaging and machine learning. *Sci Rep*. 2021;11(1):2987. [\[CrossRef\]](#)
- Collins VP, Jones DTW, Giannini C. Pilocytic astrocytoma: pathology, molecular mechanisms and markers. *Acta Neuropathol*. 2015;129(6):775-788. [\[CrossRef\]](#)
- Yamashita Y, Kumabe T, Higano S, Watanabe M, Tominaga T. Minimum apparent diffusion coefficient is significantly correlated with cellularity in medulloblastomas. *Neurol Res*. 2009;31(9):940-946. [\[CrossRef\]](#)