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Integrating Diffusion-Weighted and Perfusion-Weighted Imaging for Improved Grading and Characterization of Brain Tumors

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Abstract
This study aims to evaluate the role of Diffusion-Weighted Imaging (DWI) and Perfusion-Weighted Imaging (PWI) in the detection, characterization, and grading of brain tumors, focusing on their correlation with histopathological findings.A total of 40 patients with intracranial mass lesions underwent DWI, PWI, and conventional MRI using a 1.5 Tesla MRI scanner. Apparent Diffusion Coefficient (ADC) values were calculated for tumor core, peritumoral edema, and normal brain tissue. Cerebral Blood Volume (CBV), Cerebral Blood Flow (CBF), and Mean Transit Time (MTT) were analyzed using PWI. Data were statistically analyzed, with a p-value ≤ 0.05 considered significant.The study included 38 neoplastic lesions and 2 tuberculomas. DWI showed distinct ADC values for different tumors, with meningiomas having a mean ADC of $0.84 \pm 0.3 \times 10^{-3}$ mm²/s and schwannomas a higher ADC of 2.14×10^{-3} mm²/s. PWI revealed elevated relative CBV in high-grade gliomas (mean: 2.1 ± 0.76), while lower rCBV was observed in metastases (mean: 0.5 ± 0.26). Tuberculomas exhibited intermediate perfusion characteristics.DWI and PWI, in conjunction with conventional MRI, enhance the diagnostic accuracy for brain tumors by providing valuable information on tumor cellularity and vascularity. These techniques aid in distinguishing between tumor types, grades, and associated edema, thus improving clinical decision-making and treatment planning.

Keywords: Diffusion-Weighted Imaging (DWI), Perfusion-Weighted Imaging (PWI), Brain tumors, Apparent Diffusion Coefficient (ADC), Dynamic susceptibility contrast (DSC), Relative cerebral blood volume (rCBV), Cerebral blood flow (CBF), Tumor grading

1. Introduction:

- Brain tumors, the most prevalent primary tumors of the central nervous system (CNS), are characterized by abnormal and uncontrolled tissue growth within the brain [1]. These tumors are classified into two main categories: primary and secondary (metastatic). While metastatic brain tumors are more common among adults, brain tumors remain a leading cause of cancer-related deaths in children [2, 3, 4].
- India's incidence rates for CNS tumors are lower compared to global averages, with estimates of 2.6 per 100,000 for males and 1.6 per 100,000 for females. Despite these lower rates, mortality associated with these tumors remains significant [5, 6]. Among the various diagnostic tools,

conventional Magnetic Resonance Imaging (MRI) has been indispensable in detecting brain tumors due to its excellent soft tissue differentiation. Techniques such as T1, T2, and proton density-weighted imaging help visualize the tumor's location and size, providing morphological insights. However, conventional MRI has limitations in grading, classifying, and determining the aggressiveness of brain tumors [7].

- This is where advanced techniques, like Diffusion-Weighted Imaging (DWI) and Perfusion-Weighted Imaging (PWI), have gained importance. DWI measures water molecule diffusion within tissues, providing critical information on tumor cellularity and integrity of cell membranes. Perfusion MRI, on the other hand, evaluates the blood flow to tumors, aiding in differentiating between high-grade and low-grade tumors [8, 9]. These techniques improve tumor characterization and guide clinical decision-making.
- This study aims to assess the role of diffusion and perfusion MRI in the detection, characterization, and grading of brain tumors, focusing on their correlation with histopathological findings.

2. Materials and Methods

- The study involved a total of 40 patients who underwent both diffusion-weighted imaging (DWI) and conventional magnetic resonance imaging (MRI) of the brain. Participants were from all age groups and were referred for brain MR imaging. All scans were conducted using a Siemens Magnetom Avanto 1.5 Tesla MRI scanner. Patients with intracranial mass lesions were included, while those with metallic MRI-incompatible implants, cardiac pacemakers, metallic foreign bodies, cochlear implants, or those who were pregnant were excluded from the study.
- MR imaging included specific sequences such as T1-weighted images in axial, coronal, and sagittal planes, T2 FLAIR, and DWI sequences. The DWI sequences produced both trace and DWI images. Trace images served as the primary reference for clinical diagnosis, while apparent diffusion coefficient (ADC) maps were utilized to calculate ADC values and further investigate abnormalities detected in the trace images.
- Absolute ADC values were calculated from different tumor components, perilesional edema, and normal brain tissue. For this analysis, regions of interest (ROIs) were manually delineated, and all measurements were computed automatically, expressed in units of 10^{-3} mm^2/sec. The measured variables were analyzed as mean ADC values with standard deviation (SD). Correlation was assessed using Pearson's test, with a p-value of ≤ 0.05 considered statistically significant. The findings were thoroughly analyzed to draw final conclusions.
- Additionally, the study involved dynamic susceptibility contrast (DSC) MRI in conjunction with conventional MRI. DSC MRI measures the changes in T2* signal due to the passage of a contrast agent. The parameters for DSC MRI included:
- **Repetition Time (TR):** Short (1500-2000 ms)
- **Echo Time (TE):** Short (30-50 ms)
- **Flip Angle:** Typically between 15° to 30°
- **Slice Thickness:** 5-10 mm
- **Field of View (FOV):** Adjusted according to the region of interest
- **Matrix Size:** Usually 128x128 or 256x256
- **Temporal Resolution:** 1-2 seconds per image
- A gadolinium-based contrast agent was administered using a power injector for a rapid intravenous

bolus, typically around 0.1-0.2 mL/kg, injected at a rate of 2-4 mL/s, followed by a saline flush. Baseline images were acquired before the contrast injection, and dynamic imaging continued for a predetermined duration (1-3 min) after the contrast bolus, with additional images obtained after a delay to assess delayed enhancement as necessary.

- Using specialized software, images were reconstructed to generate perfusion maps (CBF, CBV, MTT). The perfusion data were analyzed to derive hemodynamic parameters, and qualitative assessments were performed by evaluating the images for any abnormal perfusion patterns, particularly in areas of interest.

3. Results

- The study comprised 40 patients (22 males and 18 females) aged between 6 and 69 years. Of these, 28 patients were examined for intra-axial lesions and 12 for extra-axial lesions. Among the 40 lesions identified, 38 were neoplastic, and 2 were infectious (tuberculomas).
- Out of 9 Meningioma cases, the core and wall demonstrated iso-intense signals on diffusion-weighted imaging (DWI). The mean ADC value for the core was $0.84 \pm 0.2 \times 10^{-3}$ mm²/s. The mean relative cerebral blood volume (rCBV) was 4.9 ± 2.1, with values ranging from 1.81 to 9. The lowest rCBV (1.81) was observed in a fibroblastic meningioma with xanthomatous change. The mean rCBV for perilesional edema associated with meningiomas was 1.2, ranging from 0.5 to 1.6. Cerebral blood flow (CBF) in meningiomas was 2 to 15 times higher than in normal brain tissue.In 2 Schwannoma cases, the core appeared hypointense, while the wall was hyperintense on DWI. The mean ADC for the core was 2.14×10^{-3} mm²/s, with the peripheral area showing a mean ADC of 1.10×10^{-3} mm²/s. rCBV values were found to be 2.1 and 3.5 in the two cases studied. Epidermoid cyst displayed hyperintense signals due to abnormal restricted diffusion and T2 shine-through effect, with a mean ADC of $1.08 \pm 0.12 \times 10^{-3}$ mm²/s. On perfusion imaging findings a negligible rCBV of approximately 0.2 was observed.
- The study included 21 cases of gliomas, of which 12 were low-grade gliomas (grade II), and the remaining 9 were higher-grade gliomas (grades III/IV). The DWI signal intensities of the gliomas varied, ranging from hypo- to hyperintense, without any significant trends. Nearly all grade IV gliomas exhibited heterogeneous signal patterns on DWI, with their solid components appearing hyperintense. The mean ADC value for grade II gliomas (n = 12) was $1.10 \pm 0.41 \times 10^{-3}$ mm²/s, while for grade III/IV gliomas (n = 9), it was $1.28 \pm 0.82 \times 10^{-3}$ mm²/s. ADC values for the lesion walls were calculated, showing $1.12 \pm 0.13 \times 10^{-3}$ mm²/s for grade II gliomas and $1.0 \pm 0.39 \times 10^{-3}$ mm²/s for grade III/IV gliomas. Perilesional edema was noted in both grades: for grade II gliomas, the mean ADC was $1.4 \pm 0.31 \times 10^{-3}$ mm²/s, and for grade IV gliomas, it was $1.28 \pm 0.20 \times 10^{-3}$ mm²/s (see Table 1). Relative cerebral blood volume (rCBV) ranged from 0.8 to 2.6 in grade II gliomas, with a mean of 1.6 ± 0.60, while in grade III/IV gliomas, the rCBV ranged from 0.5 to 3.5, with a mean of 2.1 ± 0.76. Edema surrounding glioblastomas showed higher rCBV values (0.8 ± 0.7) compared to grade II gliomas (0.68 ± 0.2). Additionally, cerebral blood flow (CBF) in gliomas (mean 62.1 ± 49) was greater than that of normal brain parenchyma (mean CBF in glioma cases: 30.8 ± 22.7).
- Four cases of metastasis showed the mean ADC values for the core regions of the lesions were $1.5 \pm 0.21 \times 10^{-3}$ mm²/s, while the mean ADC values for the walls measured $0.93 \pm 0.030 \times 10^{-3}$ mm²/s. The surrounding edema had a mean ADC value of $1.28 \pm 0.20 \times 10^{-3}$ mm².Metastasis had a rCBV of

0.5 ± 0.26 (range 0.2 - 0.7) with a mean CBF of 17.2 ± 6.8 ml/min/100g, indicating lower perfusion than normal brain tissue.

- Two cases of Tuberculomas were also assessed, showing a hypointense core on DWI, with iso-intense walls and hypointense edema. The mean ADC value for the Tuberculomas was 1.10 ± 0.10 x 10^{-3} mm^2/s, and the perilesional edema exhibited a mean ADC value of 1.71 ± 0.21 x 10^{-3} mm^2/s.In Tuberculomas **t**he mean rCBV was 1.5 ± 0.8 (range 1.3 - 2.4), with the lesion wall exhibiting a mean rCBV of 2.1 ± 0.6, and perilesional edema showing a mean rCBV of 1.1 ± 0.5. CBF was recorded at 36.21 ± 29 ml/min/100g, and MTT at 12.1 ± 9.1 seconds.
- On DWI, the signal intensity in the core of hemangioblastomas was hypointense with ADC value 1.9 x 10^{-3} mm^2/s (n = 1). Hemangioblastoma showed the average rCBV was 1.5 ± 0.7, with a mean CBF of 18.01 ml/min/100g and MTT of 13 seconds.

Table 1: Apparent Diffusion Coefficient in neoplastic lesions

Tumor type	ADC ($x10^{-3}$ mm2/sec)		
	Core	Wall	Edema
Meningioma	0.84 ± 0.3	0.78 ± 0.2	1.32 ± 0.1
Schwannoma	2.14 ± 0.1	2.01 ± 0.1	-
Epidermid Cyst	1.08 ± 0.12	-	-
Glioma Grade II	1.28± 0.82	1.0± 0.39	1.5± 0.20
Glioma Grade III/ IV	1.10± 0.41	1.12± 0.13	1.4± 0.31
Metastasis	1.5 ± 0.21	0.93 ± 0.03	1.28 ± 0.20
Tuberculoma	1.10 ± 0.10	-	1.28 ± 0.20
Hemangioblastoma	1.9	-	-

Table 2: Includes perfusion mapping for neoplastic lesions

Tumor type	Perfusion Mapping for Intra-axial and Extra-axial Tumor	
	rCBV	CBF (ml/min/100g)
Meningioma	4.9 ± 2.10	369.7
Schwannoma	2.8 ± 0.7	68.2
Epidermid Cyst	0.2	-
Glioma Grade II	1.6 ± 0.6	26.5
Glioma Grade III/ IV	2.1 ± 0.76	78.3
Metastasis	0.5 ± 0.76	17.2 ± 6.8
Tuberculoma	1.5 ± 0.8	36.21 ± 2.9
Hemangioblastoma	7.6 ± 1.4	382.7

Fig. 1: ADC values of different components and distribution of relative cerebral blood volume (rCBV) in neoplastic lesions

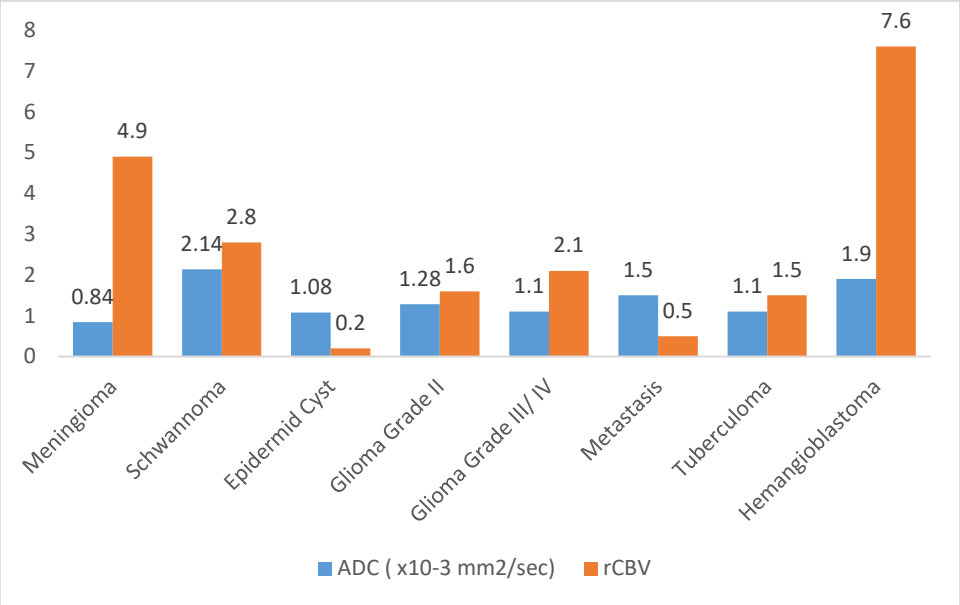
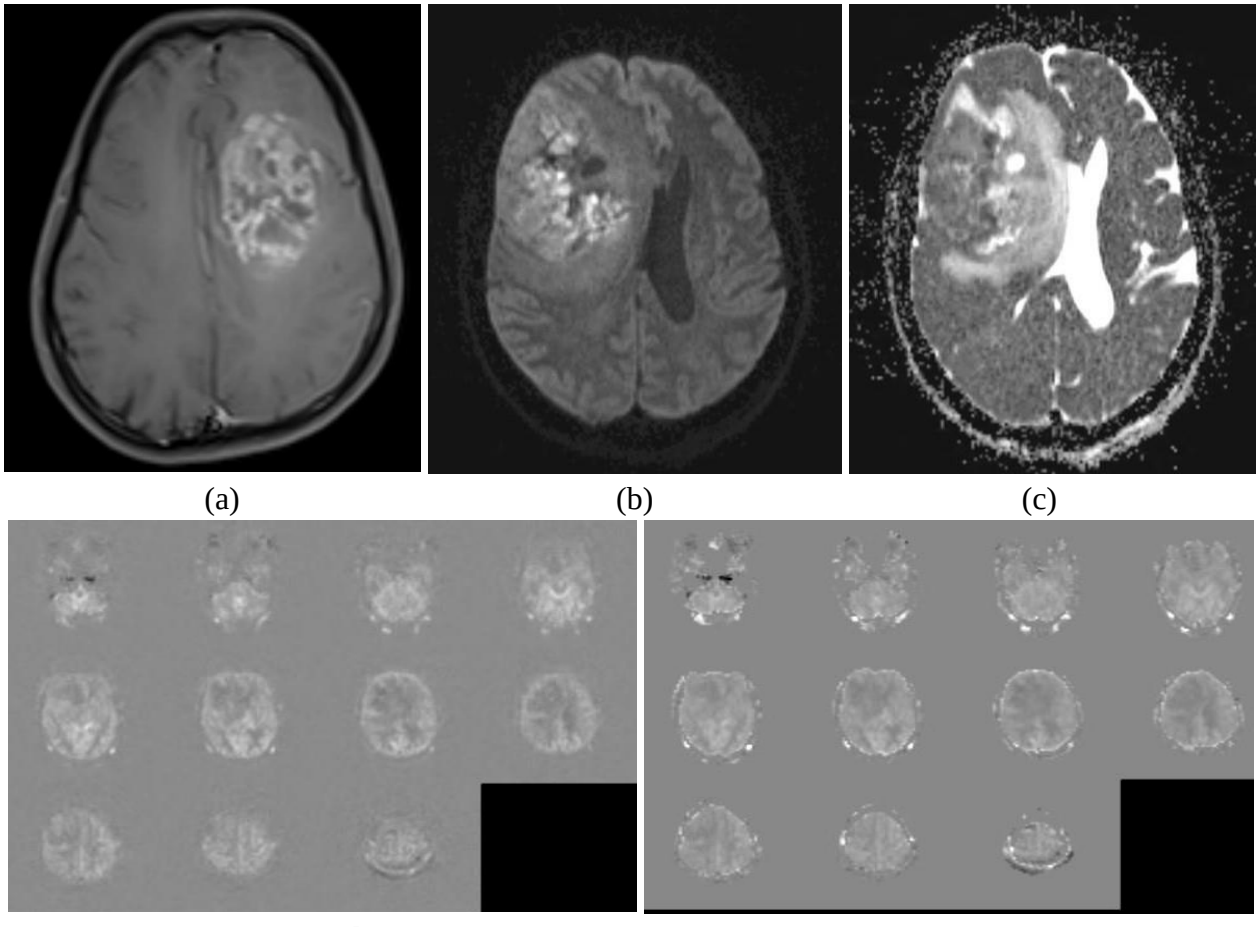


Fig. 2 A 50 year-old female patient with Glioblastoma multiforme (grade IV).
(a)Axial T1 weighted contrast enhanced image (b)Diffusion weighted image (DWI)
(c)ADC map (d)Gray scale perfusion images (e)Gray scale rCBF map



(a) (b) (c)

(d) (e)

4. Discussion

This study highlights the utility of advanced neuroimaging techniques, specifically diffusion-weighted imaging (DWI) and perfusion imaging, to characterize various brain lesions by correlating apparent diffusion coefficient (ADC) values and relative cerebral blood volume (rCBV) with underlying histological features. The results offer significant insights into the diagnosis and assessment of brain tumors, particularly in guiding clinical decision-making regarding treatment strategies.

Diffusion Imaging and ADC Values

- The study's findings regarding ADC values offer crucial insights into the cellularity and structural composition of different brain tumors. For example, benign meningiomas in our study demonstrated isointensity on DWI with elevated ADC values compared to normal brain tissue, which aligns with previous studies, including Surov et al. [9]. The increased ADC values in meningiomas can be attributed to their relatively lower cellularity and higher extracellular matrix content, which facilitates greater water diffusivity. Similarly, the lower ADC values found in Schwannomas, relative to meningiomas, are likely due to the presence of Antoni B cells, which increase tumor density and reduce water diffusion. Our results are consistent with previous findings in the literature, particularly the significant difference in ADC values between Schwannomas and meningiomas, further confirming the relationship between tumor histology and diffusion characteristics [10].
- We observed that ADC values in high-grade tumors were significantly lower compared to low-grade gliomas. The higher ADC values in low-grade tumors likely reflect increased water content in the interstitial spaces, lower cellularity, and a low nuclear-to-cytoplasmic ratio. These findings align with a study that demonstrated diffusion-weighted MRI with EPI as a valuable technique for evaluating tumor cellularity and grading gliomas [11]. The signal characteristics on DWI and ADC maps showed a strong correlation with tumor grade in pediatric brain tumors [12]. A study demonstrated that the visual analysis of diffusion-weighted images (DW) and apparent diffusion coefficient (ADC) values could effectively differentiate between low- and high-grade gliomas, showing a statistically significant difference with p-values of 0.002 and <0.001 [13]. One study found that the ADC values in gliomas (Grade II: n = 12; Grade IV: n = 8) supported similar conclusions: ADC values can be used to distinguish between different grades (Grade II > Grade IV), but they are not useful for differentiating between tumor types within the same grade [14]. Our study supports these findings; however, to investigate tumors of different types within the same grade, a larger cohort with a greater variety of tumor types would be necessary.

Perfusion Imaging

- Perfusion imaging, particularly rCBV mapping, provides valuable information about tumor vascularity and angiogenesis. Our study showed that meningiomas consistently exhibited elevated rCBV values compared to normal brain tissue, likely due to their highly vascular nature. The elevated rCBV is attributed to the presence of immature and tortuous blood vessels, which increase blood flow and contribute to higher intravascular volume. This finding supports previous research indicating that meningiomas typically show elevated perfusion parameters, aiding in the differentiation of meningiomas from other intracranial lesions [15]. Furthermore, previous studies have reported no significant correlation between mean rCBV and tumor grading. Our results align with these findings, as we also observed no significant correlation ($p > 0.05$) between rCBV/MTT and Meningioma grading [16].

- In Schwannomas, the elevated rCBV values observed in our study further confirm their vascularized nature, as documented by other studies [17]. However, despite the increased blood flow, the mean transit time (MTT) values in Schwannomas did not show significant trends compared to normal brain tissue, suggesting that increased vascularity does not necessarily correlate with prolonged blood transit times. This finding highlights the complexity of tumor hemodynamics and the need to consider multiple perfusion parameters when assessing tumor behavior.
- Research indicates that epidermoid cysts generally show reduced MRI perfusion due to their non-vascular nature [18], and our study observed similar results.
- For gliomas, our study demonstrated that rCBV values were significantly higher in high-grade gliomas compared to low-grade gliomas, in line with previous research [19, 20]. However, the lack of statistical significance in the difference between rCBV values for high- and low-grade gliomas ($p > 0.05$) may be attributed to the limited sample size in our cohort, as other studies have shown a strong correlation between increased rCBV and higher tumor grade. The elevated rCBV in high-grade gliomas is likely driven by neovascularization and the recruitment of pre-existing blood vessels, both of which are induced by tumor-derived angiogenic factors, such as VEGF. This increase in vascular permeability also contributes to the enhanced contrast observed on imaging.
- It has been observed that rCBV is significantly higher in metastasis cases, suggesting its potential as a discriminative biomarker [21]. Our study also found similar results, with elevated rCBV in metastasis cases. Interestingly, we observed significantly lower rCBV values in metastases compared to high-grade gliomas. This finding contrasts with some reports that suggest hypervascular metastases can exhibit elevated rCBV values, making differentiation from meningiomas more challenging [22]. The lower rCBV values in metastases within our study may be explained by the more cystic and less vascular nature of the metastatic lesions included in our cohort. Additionally, our study demonstrated a significant difference in rCBV values between tuberculomas and metastases, further supporting the role of perfusion imaging in distinguishing between infectious and neoplastic lesions. The elevated rCBV in tuberculomas is likely due to granulomatous inflammation and angiogenesis within the lesion, contributing to its increased vascularity.
- Finally, in hemangioblastomas, our study confirmed significantly elevated rCBV values compared to metastases, which is consistent with the literature [23]. Hemangioblastomas are highly vascular tumors, often associated with von Hippel-Lindau disease, and their elevated rCBV values reflect their rich blood supply and complex vascular architecture. This finding further underscores the importance of perfusion imaging in distinguishing between different tumor types, particularly in challenging cases where conventional imaging may be inconclusive.

5. Conclusion

Diffusion-Weighted Imaging (DWI) and Perfusion-Weighted Imaging (PWI), when combined with conventional MRI, offer invaluable non-invasive insights into the nature of brain tumors. These imaging techniques provide critical information on tumor cellularity, vascularity, and grade, helping differentiate between tumor types and predict their behavior. While DWI focuses on cellular structure via water diffusion, PWI highlights blood flow dynamics, complementing conventional MRI for comprehensive tumor assessment. The integration of these techniques into routine clinical practice could significantly improve brain tumor diagnosis and management.

6. References

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