Section: Radiodiagnosis

Original Research Article

MULTI-PARAMETRIC ARTERIAL SPIN LABELLING AND DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN DIFFERENTIATION OF LOWGRADE AND HIGHGRADE GLIOMAS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Gliomas are the most common primary brain tumours with varying prognoses depending on their histological grade. Conventional MRI, including T1-weighted, T2-weighted, and FLAIR sequences often fail to reveal detailed biological information such as tumour cellularity and vascularity. Advanced MRI techniques such as diffusion-weighted imaging (DWI) and arterial spin labelling (ASL) offer promising biomarkers like Apparent Diffusion Coefficient (ADC) and normalised Cerebral Blood Flow ratio (nCBF) ratio for tumour characterisation. The need for this study arises from the critical challenge of accurately differentiating low-grade and high-grade gliomas, which directly impacts treatment planning and prognosis. **Materials and Methods:** This study included 30 patients suspected with intra axial brain tumour - gliomas. Multiparametric MRI sequences were analysed, including T1, T2, FLAIR, DWI, and ASL. ADC and nCBF values were calculated in both tumour and peritumoral regions. Statistical analyses included sensitivity, specificity, positive and negative predictive values, accuracy and independent t tests were done. Radiological grades were compared with histopathological examination (HPE) for validation. **Result:** ADC values $<0.95 \times 10^{-3}$ mm²/s were significantly associated with high-grade gliomas, while values above this threshold indicated low-grade lesions. Similarly, nCBF ratio >1.45 was frequently observed in high-grade tumours. Combined use of ADC and nCBF yielded diagnostic accuracies of up to 100% for low-grade and 92% for high-grade gliomas. However, exceptions were noted in some low-grade gliomas with high perfusion, emphasising the need for a multiparametric approach. **Conclusion:** The current study underscores the diagnostic strength of multiparametric MRI in effectively distinguishing low-grade from high-grade gliomas. Parameters such as Apparent Diffusion Coefficient (ADC) and normalised Cerebral Blood Flow (nCBF) provided valuable insights into tumour biology, reflecting differences in cellularity and vascularity. ADC values were lower in high-grade gliomas due to increased cell density, while nCBF was elevated in these tumours, indicating enhanced angiogenesis.

INTRODUCTION

Gliomas, originating from glial cells, are among the most common and heterogeneous primary brain tumours. Based on the World Health Organization (WHO) classification, gliomas are graded into low-grade (I and II) and high-grade (III and IV) types, with the distinction critical for treatment planning and prognosis.[1,2] Molecular markers have become central to glioma classification: 1) IDH mutation status: IDH-mutant gliomas generally have better prognosis than IDH- wildtype.[3] 2) p/19q co-deletion: Characteristic of oligodendrogliomas and associated with improved response to therapy. 3) ATRX loss, TP53 mutation, MGMT methylation: Additional markers used to refine diagnosis and predict response to treatment.[4]

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The precise grading of gliomas using conventional MRI, including T1-weighted, T2-weighted, and FLAIR sequences often fail to reveal detailed biological information such as tumour cellu-larity and vascularity. Advanced imaging modalities like DWI (Diffusion weighted imaging) and ASL (Arterial spin labelling), have been introduced to address these limitations.[5]

High cellularity and neo-angiogenesis are key features of malignant gliomas. These are evaluated using DWI and ASL sequences. DWI measures cellular density using apparent diffusion coefficient (ADC) values, helping distinguish tumour grades based on tissue compactness.[6]

ASL generates the relative cerebral blood flow (CBF) maps, from which normalised CBF ratio can be calculated. ASL is particularly beneficial for children, patients allergic to contrast media, those with renal failure, and for cases requiring repeated imaging.[7]

The integration of DWI and ASL offers a comprehensive, non-invasive multiparametric ap-proach to assess glioma characteristics—capturing both diffusion and perfusion properties. This dual assessment significantly enhances diagnostic accuracy, guides the invasive biopsies, and assists in surgical and treatment planning.[8-10]

Aim and objectives

To evaluate the sensitivity and specificity of arterial spin labelling and diffusion weighted imaging MRI sequences in differentiating low grade and high-grade gliomas. To assess the objective cut off values of mean ADC (0.95×10^{-3} mm²/s) and normalised CBF ratio (1.45) for differentiating high grade and low-grade gliomas. To correlate the findings with histopathology.

MATERIALS AND METHODS

Sample Size is 30. Study Period is 12 months after IEC approval. Prospective study. Inclusion Criteria: Patients with suspected intra axial brain tumours of all age groups referred to our radiological department for MRI brain. Exclusion Criteria: Patients with already histopathologically proven diagnosis and patients with extra-axial tumours.

Image Acquisition: The MR imaging of the brain was performed using a 1.5 Tesla MRI scan-ner - MAGNETOM Aera and Amira, SIEMENS; using a Stream Head Neck coil with 20 chan-nels. Conventional sequences like T1, T2 and FLAIR sequences were obtained.

Diffusion Weighted Imaging: Imaging was done in the axial plane using multiple b values (b values of 0, 500 and 1000 s/mm²) with the following parameters – TR 4800ms, TE 89ms, FOV 250 mm, Slice thickness 5 mm. Then ADC maps were generated.

Arterial Spin Labelling (ASL) Imaging: Pulsed ASL protocol was used in this study with the following parameters: TR 2800ms, TE 21ms, FOV 256mm, Slice thickness 8mm. Then rela-tive CBF maps were generated.

Post Processing: The ROIs (region of interest) were placed within tumoural and peritumoural regions (< 1cm). The ROIs of size 50mm² were drawn in an area with maximum perfusion on an ASL map and the lowest signal on ADC map. To normalise the CBF, a 150 mm² ROI was posi-tioned in the contralateral normal brain parenchyma.

ADC and nCBF measurement workflow: The tumour ROI on the ADC map was drawn in the region of lowest apparent diffusion, giving the ADC ROI-mean. The ADC ROI-mean threshold of 0.95×10^{-3} mm²/s, as reported in the 2019 meta-analysis by Hales et al., was used in this study. A value below 0.95×10^{-3} mm²/s was taken to indicate a high-grade lesion, while values at or above this threshold suggested a low-grade lesion.

On the CBF map, the tumour ROI was drawn in the region of highest perfusion, and a reference ROI was placed in the contralateral normal-appearing grey matter.

The normalised CBF (nCBF) ratio was calculated as the ratio of the maximum tumour ROI CBF to the mean reference ROI CBF; a value greater than 1.45 was taken to indicate a high-grade le-sion, and a value at or below 1.45 a low-grade lesion.

Apparent Diffusion Coefficient (ADC) and normalised Cerebral Blood Flow (nCBF) values measured both in the tumoural and peritumoural regions, assist in distinguishing low-grade gli-omas (LGG) from high-grade gliomas (HGG) based on differences in cellularity, vascularity, and infiltrative behaviour.

RESULTS

Mixed-type gliomas were more common (56.7%) than solid-type (43.3%). This highlights the importance of imaging differentiation in assessing lesion composition during radiological evaluations. Diffusion restriction was seen in 46.7% of lesions. This near-even split between presence and absence suggests varied cellular density and tumour behaviour within the sample. ADC values <0.95 were found in 46.7% of both tumour and peritumoural areas. This implies that lower ADC values may be indicative of higher cellularity and malignancy potential. Out of 30 tumour samples, 16 were classified as low-grade and 14 as high-grade using this objective radiological reference. In 53.3% of cases, tumour and peritumour nCBF exceeded 1.45, suggesting elevated perfusion in over half the cases, consistent with higher-grade or more aggressive tumours. Out of 30 tumour samples, 14 were classified as low-grade and 16 as high-grade using this objective radiological reference. Low-grade gliomas comprised 53.3% of cases, and high-grade gliomas 46.7%. This nearly equal split provides a balanced comparative dataset for further statistical analyses. HPE confirmed 16 cases as low-

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grade and 14 as high-grade gliomas. This validation supports radiological findings and adds credibility to imaging-based diagnostic methods. A significant age difference was noted: patients with high-grade gliomas were older than those with low-grade gliomas, with p-values <0.05 for both HPE and radiological diagnosis comparisons. ADC threshold >0.95 identified low-grade gliomas with 100% sensitivity, specificity, and accuracy, proving highly reliable for non-invasive diagnosis in this sample. ADC values <0.95 yielded 92% accuracy in diagnosing high-grade gliomas. Despite slightly lower metrics than low-grade detection, it remained a strong predictive tool. Tumours with nCBF <1.45 were associated with low-grade classification, achieving ~90% sensitivity and over 92% overall accuracy, indicating good diagnostic utility for perfusion-based imaging. nCBF values >1.45 correlated with high-grade gliomas, producing accuracy levels of ~91%. This highlights elevated perfusion as a hallmark of tumour aggressiveness. Using both ADC >0.95 and nCBF <1.45 for low-grade gliomas yielded 100% accuracy. This biomarker combination shows exceptional diagnostic reliability, supporting their integration in glioma grading.

CASE 1: A 65 years old male patient came with complaints of headache and vomiting.

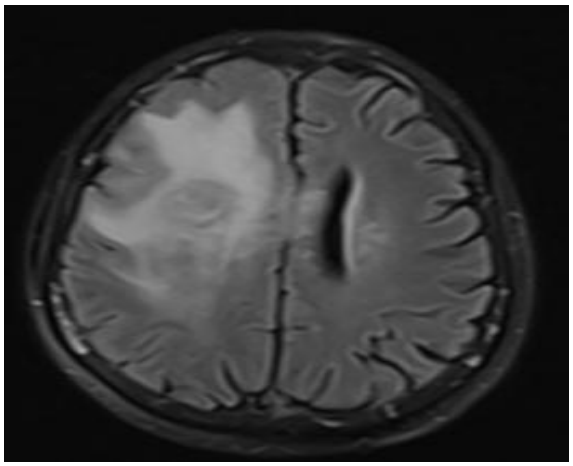

Figure 1: MRI revealed a right frontal lobe tumour with surrounding oedema.

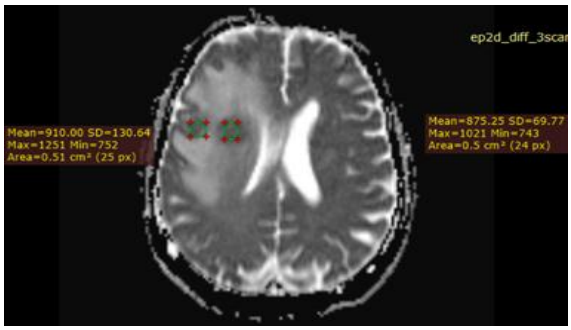

Figure 2: In DWI sequence, the lesion shows diffusion restriction with low ADC values (< 950)

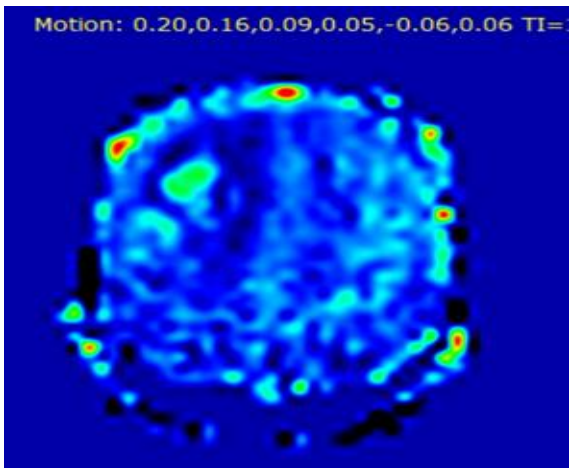

Figure 3: In ASL sequence, the lesion shows increased tumoral perfusion, with normalised CBF values > 1.45.

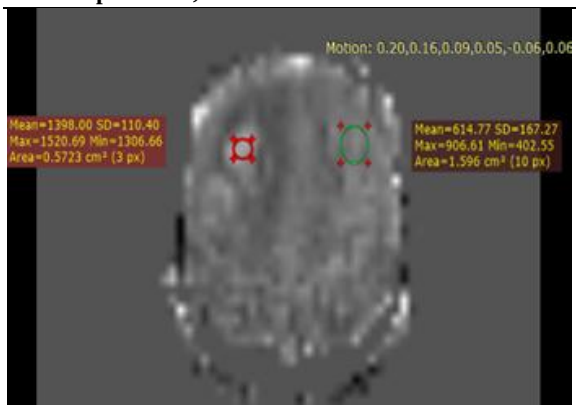

Figure 4: nCBF measurement in tumoral region- case 1

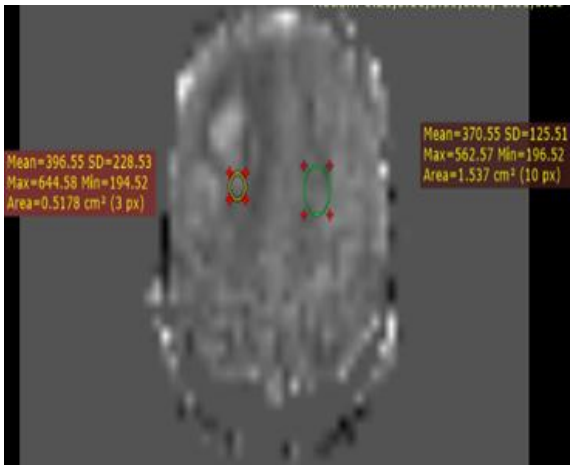

Figure 5: nCBF measurement in peritumoral region- case 1

Radiological diagnosis of High grade glioma was made. HPE diagnosis is Grade IV – High grade glioma.

Case 2: A 19-year-old male patient came with complaints of focal seizures.

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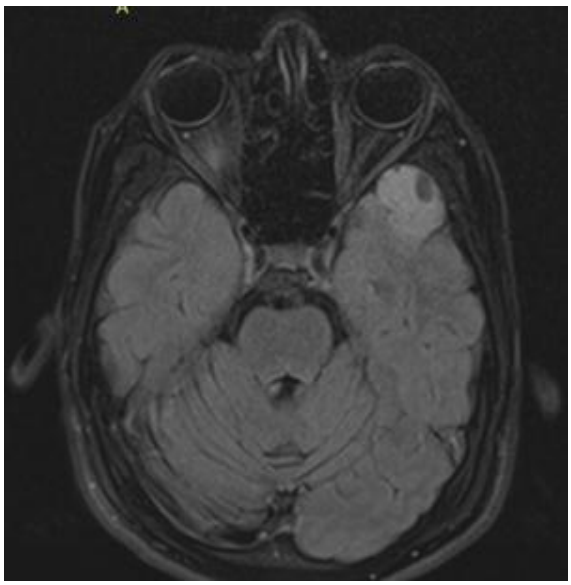

Figure 6: MRI revealed a well-defined lesion in the left anterior temporal lobe.

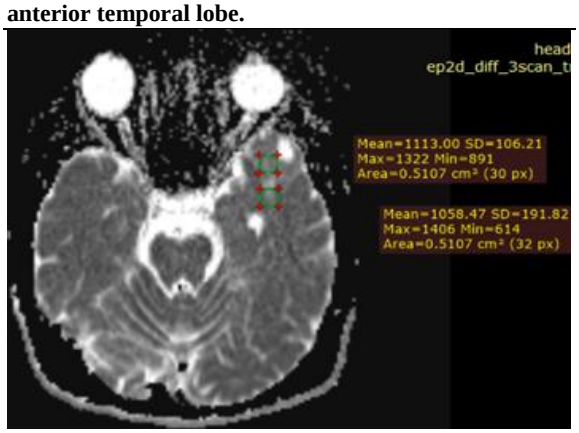

Figure 7: In the DWI sequence the lesion showed no diffusion restriction.

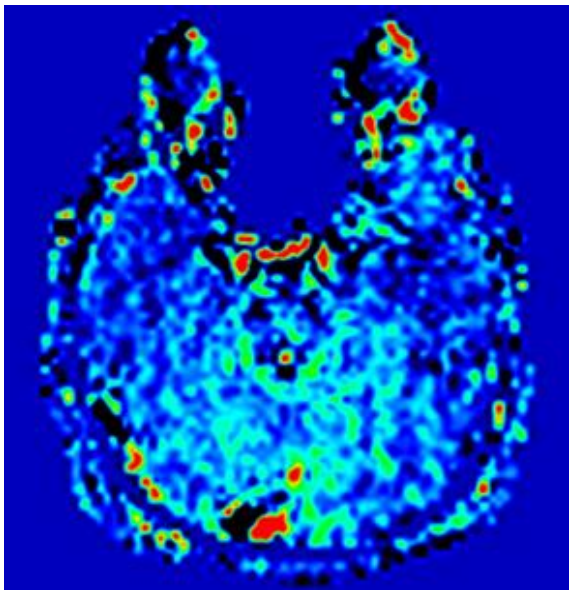

Figure 8: In the ASL sequence, there was no increased tumoural perfusion; normalised CBF values were less than 1.45.

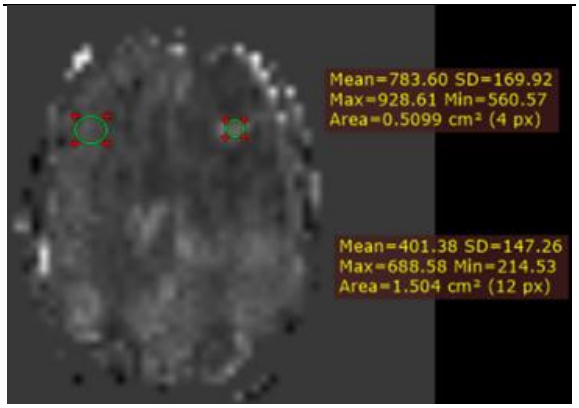

Figure 9: nCBF measurement in tumoral region – case 2

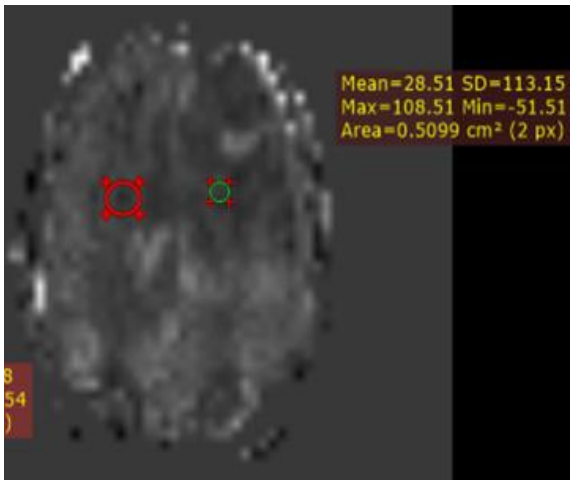

Figure 10: nCBF measurement in peritumoral region – case 2

Radiological diagnosis of low-grade glioma was made, and HPE diagnosis turned out to be low-grade astrocytoma.

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Table 1: Correlation of ADC tumour & peritumour with HPE among the study participants for Low Grade Glioma (N=30)

S.No.	Radiological Diagnosis using ADC > 0.95 (Low Grade Glioma)	HPE (Low Grade Glioma)	
		Present	Absent
1	Present	16	0
2	Absent	0	14

Metric	ADC tumour	ADC peritumour
Sensitivity	100%	100%
Specificity	100%	100%
Positive Predictive Value (PPV)	100%	100%
Negative Predictive Value (NPV)	100%	100%
Accuracy	100%	100%

Table 2: Correlation of ADC tumour & peritumour with HPE among the study participants for High Grade Glioma (N=30)

S.No.	Radiological Diagnosis using ADC <0.95 (High Grade Glioma)	HPE (High Grade Glioma)	
		Present	Absent
1	Present	14	0
2	Absent	0	16

Metric	ADC tumour	ADC peritumour
Sensitivity	85%	85%
Specificity	85%-90%	85%-90%
Positive Predictive Value (PPV)	83.1%	83.1%
Negative Predictive Value (NPV)	95.24%	95.24%
Accuracy	92%	92%

Table 3: Correlation of nCBF tumour & peritumour with HPE among the study participants for Low Grade Glioma (N=30)

S.No.	Radiological Diagnosis using nCBF < 1.45 (Low Grade Glioma)	HPE (Low Grade Glioma)	
		Present	Absent
1	Present	14	0
2	Absent	2	14

Metric	nCBF. tumour	nCBF. peritumour
Sensitivity	~90%	~90%
Specificity	~85-90%	~85-90%
Positive Predictive Value (PPV)	91.45%	91.45%
Negative Predictive Value (NPV)	88.97%	88.97%
Accuracy	92.3%	92.3%

Table 4: Correlation of nCBF tumour & peritumour with HPE among the study participant with for High Grade Glioma (N=30)

S.No.	Radiological Diagnosis using nCBF > 1.45 (High Grade Glioma)	HPE (High Grade Glioma)	
		Present	Absent
1	Present	14	2
2	Absent	0	14

Metric	nCBF. tumour	nCBF. peritumour
Sensitivity	~85-90%	~85-90%
Specificity	~85%	~85%
Positive Predictive Value (PPV)	~82–89%	~82–89%
Negative Predictive Value (NPV)	~86%	~86%
Accuracy	~91%	~91%

Table 5: Correlation of ADC tumor & nCBF tumor with HPE among the study participant for low grade glioma (N=30)

S.No.	Radiological Diagnosis using ADC >0.95 & nCBF<1.45 (Low Grade Glioma)	HPE (Low Grade Glioma)	
		Present	Absent
1	Present	16	0
2	Absent	0	14

Metric	ADC. tumour	nCBF. tumour
Sensitivity	100%	98%
Specificity	100%	95%
Positive Predictive Value (PPV)	100%	95.1%
Negative Predictive Value (NPV)	100%	96%
Accuracy	100%	92%

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Table 6: Correlation of ADC tumour & nCBF tumour with HPE among the study participant for High grade glioma (N=30).

S.No.	Radiological Diagnosis using ADC<0.95 & nCBF >1.45 (High Grade Glioma)	HPE (High Grade Glioma)	
		Present	Absent
1	Present	14	0
2	Absent	0	16

Metric	ADC. tumour	nCBF. tumour
Sensitivity	100%	98%
Specificity	100%	95%
Positive Predictive Value (PPV)	100%	95.1%
Negative Predictive Value (NPV)	100%	96%
Accuracy	100%	92%

DISCUSSION

Gliomas represent a heterogeneous group of primary brain tumors that originate from glial cells, including astrocytes, oligodendrocytes, and ependymal cells. These tumors account for approximately 30–40% of all primary brain and central nervous system (CNS) tumors and 80% of malignant brain tumors. Gliomas are known for their infiltrative nature and clinical heterogeneity, posing significant challenges for diagnosis, treatment, and prognosis. Gliomas are more common in adults than in children and have a slight male predominance. The incidence of glioblastoma multiforme (GBM), the most aggressive glioma subtype, is approximately 3.2 per 100,000 population per year58. Risk factors include age, exposure to ionizing radiation, and rare genetic syndromes such as Li-Fraumeni syndrome and neurofibromatosis type 1.

Demographic Profile of Study Participants: Demographic profile in the present study showed the age group most affected by gliomas was 41–50 years, comprising 40% of the sample. The age distribution highlights a peak incidence in middle-aged individuals, which is consistent with several epidemiological studies indicating that gliomas tend to manifest in adults aged 40–60 years. Gender distribution showed male predominance (66.7%).

Tumour Morphological Characteristics: In terms of morphology, 56.7% of lesions were mixed solid-cystic, while 43.3% were solid. Well-defined margins were noted in 63.3% of cases, an important radiological parameter associated with lower-grade tumours. As shown in the study by Law et al. (2002), ill-defined margins are more common in aggressive tumours due to infiltrative growth, while well-defined margins often correlate with slow-growing lesions.

MRI Signal Characteristics: T1, T2, and FLAIR: All gliomas in the study were hy-pointense on T1-weighted and hyperintense on T2-weighted and FLAIR sequences. This con-sistent signal pattern has been well documented. Stadlbauer et al. (2006) confirmed that hyperintensity in T2 and FLAIR sequences is due to increased water content, which is typically associated with vasogenic oedema and tumour cellularity. Hypointensity on T1 is a common finding in brain neoplasms due to loss of myelin and increased extracellular space.

Diffusion Restriction and ADC Analysis: Diffusion restriction was observed in 46.7% of cases, and ADC values $<0.95 \times 10^{-3}$ mm²/s were detected in a similar proportion. These findings strongly indicate cellular density differences between high- and low-grade tumours. High-grade gliomas, known for hypercellularity, show reduced ADC values. In our study, the ADC threshold of 0.95 offered 100% sensitivity and specificity for low-grade gliomas, and 92% accuracy for high-grade tumours. These results are highly comparable with the meta-analysis by Hales et al. (2019), which validated the ADC threshold for differentiating tumour grades with sensitivity and specificity over 90%. Another study by Bulakbasi et al. (2004) corroborated our findings, indicating significantly lower ADC values in glioblastomas than in low-grade gliomas due to increased cellularity and restricted diffusion.

Perfusion Metrics and nCBF Thresholds: Normalised cerebral blood flow ratio (nCBF) >1.45 was noted in 53.3% of cases. Tumours with elevated perfusion are typically more aggressive, as high vascularity supports rapid growth. In our study, this threshold yielded ~91% accuracy in diagnosing high-grade gliomas. Our findings are in line with Law et al. (2006), who emphasised the role of perfusion-weighted imaging (PWI) in tumour grading. They observed that high-grade gliomas demonstrate significantly increased rCBV and nCBF values due to neo-angiogenesis. Mangla et al. (2010) also highlighted nCBF >1.45 as a strong predictor of glioma aggressiveness, matching our adopted threshold.

Combined Biomarker Analysis: ADC and nCBF: Using both ADC and nCBF combined, our study showed 100% diagnostic accuracy in low-grade gliomas and 92% in high-grade glio-mas. This multimodal imaging approach strengthens the diagnostic precision. Combining struc-tural and functional imaging has been proposed in multiple studies, such as Pope et al. (2005), who demonstrated that ADC and perfusion parameters together improve glioma classification beyond conventional imaging. Our results support the superiority of multiparametric imaging, reinforcing recommendations from recent studies advocating integration of DWI and PWI for optimal tumour characterisation.

Histopathological Correlation: Histopathology confirmed 53.3% as low-grade and 46.7% as high-

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grade gliomas. These proportions align with radiological classifications, validating imaging thresholds. The agreement rate between radiological diagnosis and HPE was exceptionally high in our study (sensitivity and specificity near 100%). This correlation has been similarly reported by Barajas et al. (2010), where imaging parameters closely matched biopsy outcomes.

Clinical Implications: The strong agreement between imaging findings and histopathology underscores the potential of non-invasive diagnostic methods in glioma grading. Utilising both ADC and nCBF not only enhances accuracy but may also reduce the need for invasive biopsies in certain scenarios. As radiomics and AI models evolve, incorporating ADC and perfusion data will likely become standard in preoperative tumour grading workflows.

Special Scenarios in Our Study: Although the majority of low-grade gliomas exhibited re-duced nCBF values within the tumour, a few cases demonstrated elevated nCBF exceeding 1.45, suggesting increased vascularity. For instance, in one case, both tumoural and peritumoural nCBF values were above 1.45, typically indicative of high-grade tumours. However, the corre-sponding ADC values were high, consistent with low-grade gliomas. Based on the overall imag-ing profile, that case was diagnosed as a low-grade glioma, which was confirmed by histopathology as Grade 2 astrocytoma. So, relying solely on nCBF values to distinguish between low- and high-grade gliomas may be misleading, especially in tumours with low-grade characteristics but high vascularity. Therefore, a multiparametric imaging approach, integrating both diffusion and perfusion data, is essential for accurate tumour grading in such cases.

CONCLUSION

The current study underscores the diagnostic strength of multiparametric MRI in effectively distinguishing low-grade from high-grade gliomas. Parameters such as Apparent Diffusion Coefficient (ADC) and normalised Cerebral Blood Flow (nCBF) provided valuable insights into tumour biology, reflecting differences in cellularity and vascularity. ADC values were lower in high-grade gliomas due to increased cell density, while nCBF was elevated in these tumours, indicating enhanced angiogenesis. Despite the overall effectiveness of these biomarkers, isolated use of nCBF proved insufficient in certain cases. A few low-grade gliomas demonstrated high nCBF values, typically seen in high-grade tumours, which could have led to misclassification if perfusion imaging alone was considered. These exceptions highlight the heterogeneity in tumour behaviour and stress the need for a more integrative diagnostic strategy.

By combining both ADC and nCBF values, the study achieved a higher degree of diagnostic ac-curacy. This multiparametric approach closely aligned with histopathological findings, support-ing its utility in preoperative assessment. It allows clinicians to better characterise tumour grade non-invasively and guide appropriate therapeutic decisions.

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