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ORIGINAL ARTICLE

Assessment of PSR as a Novel Parameter in Perfusion Imaging for CNS Tumor Characterization: An Observational Study

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Abstract

Introduction: Magnetic resonance imaging (MRI) has emerged as the primary modality for diagnosing and evaluating central nervous system (CNS) tumors, transitioning from structural to functional assessment. Advanced MRI techniques, including MR spectroscopy and perfusion imaging, offer insights into functional, metabolic, and hemodynamic changes in addition to structural abnormalities. The study aims to assess the role of PSR (Post-Contrast Signal Recovery) alongside rCBV (Relative Cerebral Blood Volume) and rPSR (Relative Percentage of Signal Recovery) in differentiating grade IV glioma, solitary brain metastasis, and primary CNS lymphoma. **Materials and Methods:** An observational study was conducted on 38 patients with lymphoma, metastases, and grade IV glioma, utilizing DSC (Dynamic Susceptibility-Weighted Contrast-Enhanced) perfusion imaging and histopathology reports. Sociodemographic, clinical, and MRI parameters were collected. PSR measurements were obtained from perfusion maps using dedicated software. Statistical analysis was performed using SPSS version 27.0. **Results:** Among the study population, the mean age was 54.16±12.47, with male predominance (63.2%). Conventional imaging characteristics revealed significant differences, including T2 hypo intensity in lymphoma and FLAIR hyperintensity in all gliomas. Perfusion parameters showed higher rCBV in metastases and grade IV glioma compared to lymphoma, whereas PSR and rPSR were higher in lymphoma. PSR and rPSR effectively differentiated among the tumor types ($p<0.001$). **Conclusion:** Our study underscores the critical role of advanced MRI techniques, particularly DSC perfusion imaging, in differentiating between grade IV gliomas, solitary brain metastases, and primary CNS lymphomas. PSR emerges as a valuable parameter alongside rCBV and rPSR, demonstrating potential for accurate tumor characterization.

Keywords: Magnetic resonance imaging, CNS tumors, PSR, rCBV, rPSR

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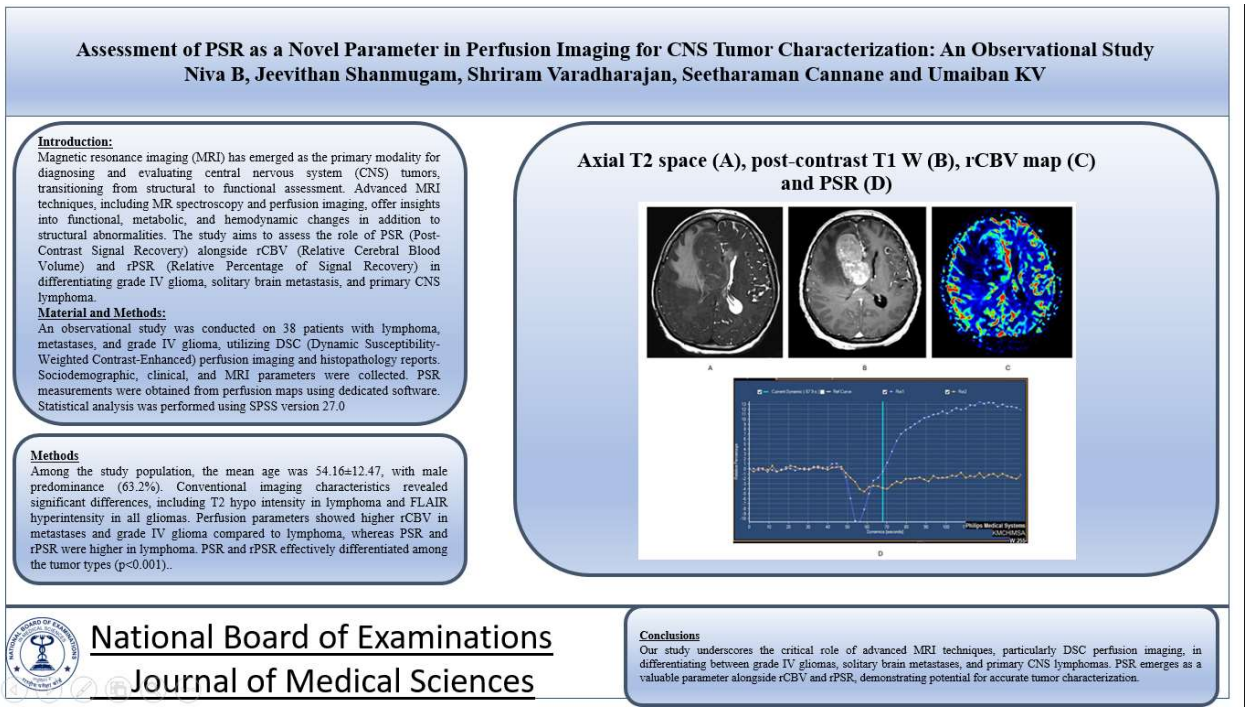
Graphical Abstract



Introduction

Magnetic resonance imaging (MRI) after its widespread availability has evolved as the imaging modality of choice in the diagnosis and evaluation of CNS tumors. The role of neuroimaging in brain tumors has advanced from purely structural to functional imaging. Apart from assessing structural abnormality and tumor-related complications, MRI is also used to identify functional, metabolic, hemodynamic, cellular, and cytoarchitectural changes. Advanced MRI techniques are now commonly used in the evaluation of brain tumors. These include MR spectroscopy for metabolite assessment and perfusion imaging for microvascular characterization. Often these advanced imaging techniques are useful in predicting the grade of the neoplasm and its biological behavior, especially given the recent modifications in the WHO classification. These may in the future be incorporated into radiogenomic signatures. In 2016, the World Health Organization revised its basic classification of primary brain tumors to incorporate genetic information and molecular status superseding histological grade.

There is considerable intersect in the conventional MRI appearances of common intracranial malignant lesions, such as gliomas, metastases, and lymphoma. Early Prompt diagnosis is important as management differs in these three groups. Although the histopathological examination is the gold standard for the diagnosis of brain tumors, it carries an inherent risk of sampling bias. Molecular status and advanced imaging can therefore supplement routine work up such as conventional imaging for more accurate diagnosis and prognostication. Therefore, newer techniques in MRI should

be utilized to differentiate between these various brain tumors.

Dynamic susceptibility-weighted contrast-enhanced (DSC) MRI is a perfusion imaging that is used to assess the capillaries and microvascular characteristics of these tumors. Relative cerebral blood volume (rCBV) is a commonly used perfusion parameter that is a marker of vascularity and neo-angiogenesis in brain tumors. It is considered as one of the most important hemodynamic variables used in the characterization of tumors. In lymphomas, rCBV is lower than in gliomas and metastases owing to the lack of neo-angiogenesis. However, rCBV values often overlap in gliomas and metastases. Percentage of signal recovery (PSR), which is a lesser utilized DSC derived parametric, plays an important role in such cases.

PSR, or Post-Contrast Signal Recovery, denotes the proportion of signal intensity regained following the initial administration of contrast relative to the baseline signal intensity (before contrast administration). Initially, there is a decline in signal intensity after the contrast agent is administered, which gradually reverts towards the baseline due to the first pass circulatory effect. The extent of this recovery determines the PSR value and is influenced by various factors such as contrast agent leakage, extravascular space size, and blood flow rate [1-6].

There are reports of low values of PSR in metastatic lesions, intermediate in glioblastoma (GBM), and high (overshooting) in primary central nervous system lymphomas (PCNSL). The relative percentage of signal recovery (rPSR) is a related parameter whose role is still under evaluation. Hence in this study, we wanted to evaluate the role of PSR as compared to rCBV and rPSR in differentiating grade IV glioma, solitary brain metastasis, and primary CNS lymphoma.

Materials and Methods

We conducted an observational study in the Department of Radiology, Kovai Medical Centre and Hospital, Coimbatore. In our study, 38 patients with lymphoma, metastases, and grade IV glioma with optimum DSC perfusion imaging and histopathology report during the period of August 2019 to July 2021 were included after discussing with the participants about the need for the study, objectives and other ethical issues concerned. Patient information was given to the participant. Ample time was given to the study participant for understanding the study. Once they agreed to participate, written informed consent was obtained. A structure clinical proforma was designed for the study. Sociodemographic variables, clinical history/ findings and MRI parameters were elicited. None of the lymphoma patients had signs of immunosuppression and no patient had signs of systemic involvement. Only patients with solitary metastasis were included in this study.

Exclusion criteria included general contraindications for MRI, incomplete studies due to various reasons like an uncooperative patient, poor image quality, and extensive artifacts. Those who had contraindication for MRI contrast were also excluded.

Imaging was performed with either a 1.5 T [Ingenia; Philips Medical Systems] or 3T [MAGNETOM Skyra; Siemens Healthcare]. Our tumor protocol included T1 in three orthogonal planes, coronal T2, axial T2 FLAIR, SWI, DWI axial, ADC, MR spectroscopy, and post-contrast T1 images in all 3 planes. Using a gradient recalled T2*weighted echo-planar imaging sequence (ep2d_perf), DSC imaging was performed.

Parameters used in 1.5 T were as follows:

- TR/TE of 2341/40 ms,
- FOV of 220 mm,
- Voxel size of 2.4 x 2.4 x 5 mm,
- Slice thickness of 5 mm.
- A total of 30 image volumes each with 40 image sets were acquired (a total of 1200 images), in which the first 5 image volumes were acquired before starting the contrast agent injection to establish a pre-contrast baseline. At the end of the 5th image volume, 0.1-0.2mmol/kg gadolinium contrast was injected using a power injector at a rate of 2.5-3 ml/s through an 18 or 20 G intravenous catheter. This was immediately followed by a bolus injection of saline (a total of 20 ml at the same flow rate).

Parameters used in 3 T were as follows:

- TR/TE of 2340/30 ms,
- FOV of 220 mm,
- Voxel size = 1.7 x 1.7 x 4 mm,
- Slice thickness= 4 mm.
- A total of 30 image volumes each with 60 image sets were acquired (a total of 1800 images), in which the first 5 image volumes were acquired before starting the contrast agent injection to establish a pre-contrast baseline. At the end of the 5th image volume, 0.1-0.2mmol/kg gadolinium contrast was injected using a power injector at a rate of 2.5-3 ml/s through an 18 or 20 G intravenous catheter. This was immediately followed by a bolus injection of saline (a total of 20 ml at the same flow rate).

PSR measurement

All perfusion data were transferred to a stand-alone workstation for post-processing using dedicated advanced software packages [Neuro Perfusion Evaluation, Syngo multimodality workplace (MMWP) VE61B, Siemens Healthcare Gmbh, Germany or T2* MR Neuro Perfusion, IntelliSpace Portal (ISP) Version 9.0, Philips Medical Systems Netherlands B.V.]. From the processed perfusion images color-coded CBV maps were obtained. For PSR measurement, an ROI (Region of Interest) of 25-40 mm^2 was drawn on the perfusion maps carefully excluding areas of necrosis or hemorrhage. The signal intensity curves were thus obtained and the PSR value was calculated as follows:

$$PSR = 100\% \times (S_1 - S_{min})/ (S_0 - S_{min})(1,2),$$

Where,

S_0: baseline pre-contrast T2*W signal intensity.

S_1: recovered post-contrast T2*W signal intensity.

S_{min}: minimum T2*W signal intensity

Another ROI was simultaneously placed in the contralateral normal-appearing brain and rPSR was calculated as follows:

rPSR= PSR (lesion)/PSR (contralateral normal brain)(3).

Statistical analysis

The data were entered into MS Excel and analyzed using Statistical Package for Social Sciences (IBM SPSS) version 27.0. Sociodemographic variables were analyzed as proportions or percentages for categorical variables, either mean ± SD or Median (IQR) were analyzed for numerical variables. The difference in mean between the different types of tumors was analyzed using the Kruskal Wallis test. A Chi-square test was used to analyze the relationship between various study variables and different types of tumors. The p-value <0.05 was considered statistically significant.

Results

A total of 38 patients including 24 high-grade IV gliomas, 7 primary CNS lymphomas (PCNSLs), and 7 brain metastases were included in the study. In our study, the mean age of the participants was 54.16±12.47. Out of 38 patients, 24 (63.2%) were male and 14 (36.8%) were female. The most common location of the tumors included in our study was frontal parenchyma (47.4%). Baseline signal characteristics on conventional imaging were analyzed. Lymphoma was the only tumor to show frank T2 hypointensity more commonly while all gliomas showed FLAIR hyperintensity (Table 1). Thus, these signal characteristics on the T2 weighted image and FLAIR were found to be statistically significant. Among the various other p

arameters studied, SWI blooming and cystic necrosis were also found to be statistically significant. Blooming on SWI was found in 45.8% of patients in the grade IV glioma group and 85.7% in the metastases group. Cystic necrosis was present in 45.8% of patients in the grade IV glioma group and 85.7% in the metastases group (Table 1). Figures 1, 2 and 3 show the representative conventional images of a case of CNS lymphoma, solitary brain metastasis, and grade IV glioma.

Among perfusion parametrics, the mean rCBV value was higher in metastases (3.23±0.51) and grade IV glioma (3.08±0.67), whereas low in lymphoma (1.14±0.25) with a p-value of <0.001. The mean PSR value was lower in metastases (56.03±7.87) and grade IV glioma (80.69±6.48), whereas higher in lymphoma (146.13±40.97) with a p-value of <0.001. The mean rPSR value was lower in metastases (0.69±0.03) and grade IV glioma (0.92±0.05), whereas higher in lymphoma (1.84±0.68) with a p-value of <0.001, which is statistically significant. In our study, we found that PSR and rPSR values can differentiate lymphoma, metastases, and grade IV glioma lesions (Table 2).

Chi-square test was done for various categorical variables measured to find out if any association is present with the HPE diagnosis. There was no significant difference between the HPE diagnosis and sex, Laterality, Location of tumor, supra/ infratentorial region, Predominant signal on T1, Diffusion restriction of solid component and Lipid Lactate Peak.

Table 1. Distribution of study population according to Socio demographic and clinical variables

Variables	HPE						χ^2 Value	p Value
	Lymphoma		Grade IV glioma		Metastases			
	n=7	%	n=24	%	n=7	%		
Age								
≤60	3	42.9	18	75	6	85.7	3.620	0.164
>60	4	57.1	6	25	1	14.3		
Sex								
Male	6	85.7	14	58.3	4	57.1	1.880	0.391
Female	1	14.3	10	41.7	3	42.9		
Predominant signal on T1 weighted image								
Hypointense	4	57.1	15	62.5	2	28.6	2.536	0.281
Isointense	3	42.9	9	37.5	5	71.4		
Predominant signal on T2 weighted image								
Hypointense	1	14.3	0	0	0	0	11.283	0.024
Isointense	1	14.3	0	0	2	28.6		
Hyperintense	5	71.4	24	100	5	71.4		
Signal on Flair								
Hyperintense	5	71.4	24	100	5	71.4	7.664	0.022
Isointense	2	28.6	0	0	2	28.6		
Perilesional edema								
Mild	1	14.3	13	54.2	0	0	12.722	0.013
Moderate	5	71.4	10	41.7	4	57.1		
Marked	1	14.3	1	4.2	3	42.9		
SWI blooming	0	0	11	45.8	6	85.7	10.433	0.005
Cystic necrosis	0	0	11	45.8	6	85.7	10.433	0.005
Diffusion restriction of solid component	7	100	22	91.7	6	85.7	1.000	0.607
Lipid lactate peak	4	57.1	6	30	4	80	4.717	0.095
Enhancement of solid component	5	71.4	21	87.5	7	100	2.252	0.283

Table 2. Comparison of Mean rCBV, PSR, rPSR with HPE diagnosis

HPE	**Maximum rCBV**			**PSR**			**rPSR**		
	Mean	**SD**	**Median (IQR)**	**Mean**	**SD**	**Median (IQR)**	**Mean**	**SD**	**Median (IQR)**
Lymphoma	1.14	0.25	1.03 (0.96-1.46)	146.13	40.97	150 (106.1-186.7)	1.84	0.68	2.05 (1.04-2.42)
Grade IV glioma	3.08	0.67	3.06 (2.52-3.70)	80.69	6.48	81.65 (75.53-86.83)	0.92	0.05	0.92 (0.91-0.96)
Metastases	3.23	0.51	3.04 (2.88-3.72)	56.03	7.87	53.4 (51.6-62.8)	0.69	0.03	0.70 (0.67-0.71)
Kruskal Wallis Value	17.077			26.742			20.401		
p Value	<0.001			<0.001			<0.001		

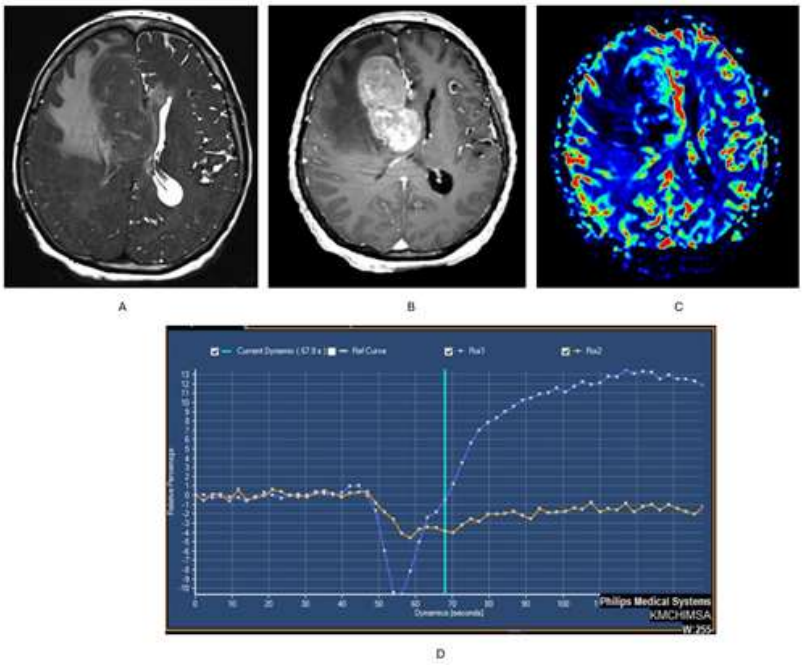


Figure 1: Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of lymphoma show a well-defined solid intra-axial mass lesion involving the right parasagittal frontal parenchyma which appears relatively hypointense on T2, shows heterogeneous enhancement, relative hypoperfusion with few eccentric areas of raised rCBV and high PSR with overshooting.

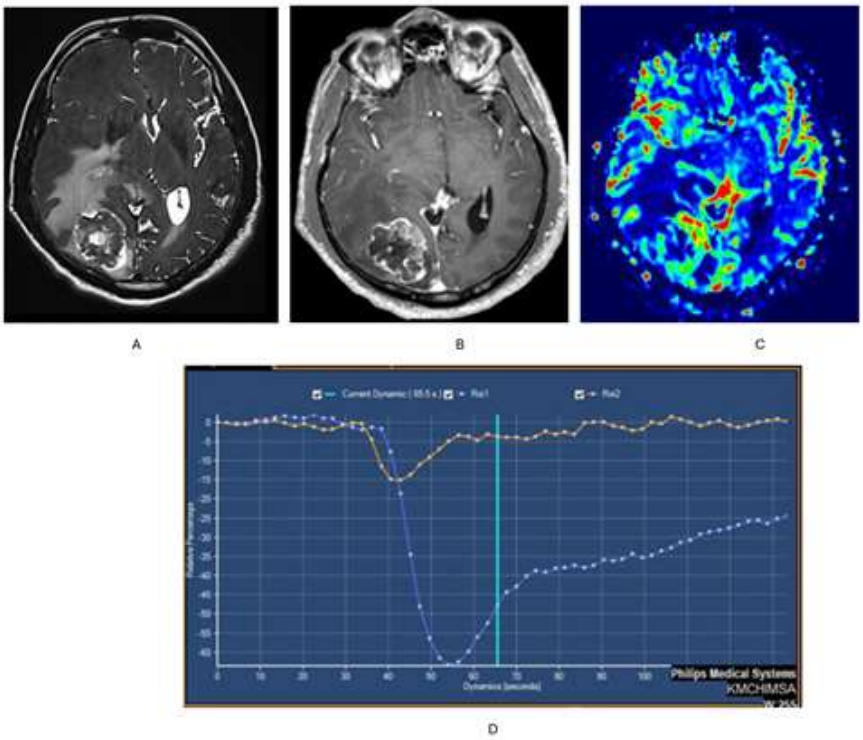


Figure 2. Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of solitary brain metastasis show an irregular solid intra-axial lesion in the right occipital lobe. It appears heterointense on T2 with central cystic area, enhancement of solid component on post-contrast images, increased perfusion in enhancing component and low PSR

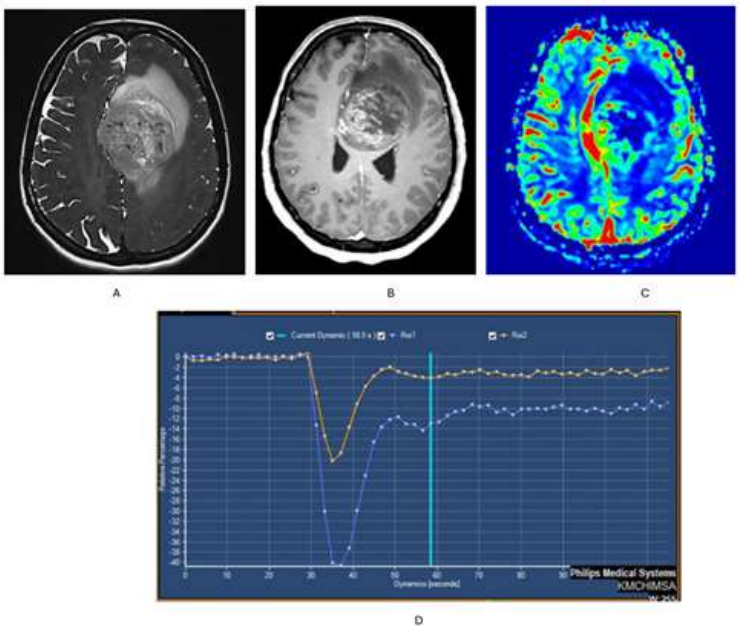


Figure 3. Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of glioblastoma show an ill-defined infiltrative intra-axial left parasagittal lesion involving superior frontal and cingulate parenchyma which appears heterointense on T2, shows heterogenous post-contrast enhancement with internal necrosis and anterior non-enhancing areas, increased perfusion in enhancing component and intermediate PSR.

All those who were diagnosed with Glioma had hyperintensity on T2 and FLAIR compared to 71.4% in lymphoma and metastasis. SWI blooming and cystic necrosis was not present in Lymphoma, it was present in 45.8% of Glioma and 85.7% in Metastasis.

Discussion

In this study, we looked at the role of T2* MRI perfusion imaging, focusing on the lesser utilized parametric namely the percentage signal recovery (PSR) in the differentiation of the various malignant brain tumors, and compared its diagnostic accuracy with the more commonly used perfusion parameter, relative cerebral blood volume. This study included high-grade gliomas (Grade IV gliomas/GBMs), CNS lymphomas, and solitary metastases. Accurate diagnosis of these tumors is crucial for preoperative treatment planning and prognostication. There is a substantial difference in management strategies for these brain tumors. Although histopathology is the gold standard, surgical methods are invasive and even within certain tumors have sampling bias. Pre-operative diagnosis can help the surgeon decide on the optimal treatment strategy. Although conventional MRI helps narrow down the differential diagnosis of a brain tumor, its diagnostic accuracy in their differentiation is low and can be increased using advanced imaging methods such as perfusion and spectroscopy. Considerable overlap exists in the signal characteristics on conventional sequences among these tumors. Advanced imaging adds as an adjunct in further narrowing the differential and excluding certain tumors on many occasions. Among the various perfusion methods, T2* is the most used technique, and relative cerebral blood volume is the most common parameter studied. Although percentage signal recovery has been additionally studied as a parameter in various previous studies, it has not been routinely incorporated into the imaging guidelines and practice protocols. In our study, we have included advanced perfusion parameters of the common brain tumors namely grade IV glioma, PCNSL, and solitary brain metastases. We aimed to evaluate their role in the accurate diagnosis of these brain lesions. We have also tried to compare the diagnostic accuracy of the perfusion parameters like rCBV, PSR, and rPSR using histopathology as the gold standard.

In our study, almost all the grade IV glioma and lymphoma cases were supratentorial in location. This correlates well with other studies in the past which have also shown that nearly all GBMs were localized to the supratentorial parenchyma [7].

With respect to signal characteristics, T2 and FLAIR signals were found to be discriminatory. It also varies according to the immune status. Prior literature has shown that the T2 hypointensity usually seen in lymphomas may be attributed to the high nuclear-cytoplasmic ratio [8]. All grade IV gliomas in this study showed hyperintense signal on FLAIR as compared to 70% of the other two groups, which was statistically significant. This is similar to a prior study done by Elghany et al. [9], where the majority of GBM (98.1%) were hyperintense.

It is important to differentiate PCNSL from other tumors as the first line of treatment for lymphoma is chemotherapy and not surgical resection [10]. We have found that PCNSL has low rCBV as well as higher PSR and rPSR values. Possibly here, the T1 effect is dominant over the T2* effect leading to the overshoot above baseline. Other factors like cellularity, blood volume, and vascular permeability may also have a role in this [11-13]. Even though the signal intensity curve of PCNSL showed characteristic overshoot, the diagnostic performance of rCBV was found to be better than PSR. Nonetheless, both the parameters were significant with varying thresholds.

Due to the significant overlap of the perfusion values in gliomas and metastases, rCBV was not sensitive enough to differentiate between grade IV glioma and metastases with similar higher values. However, the mean PSR was statistically significant among these groups. We reckon that metastases produce more pronounced T2* effects due to prominent capillary fenestration and the lack of BBB integrity, whereas high-grade gliomas demonstrate moderate T2* effects due to lesser capillary fenestration and partial disruption of BBB components [14-16].

Conclusion

Our study underscores the critical role of advanced MRI techniques, particularly DSC perfusion imaging, in differentiating between grade IV gliomas, solitary brain metastases, and primary CNS lymphomas. PSR emerges as a valuable parameter alongside rCBV and rPSR, demonstrating potential for accurate tumor characterization. These findings emphasize the significance of incorporating advanced imaging modalities into routine clinical practice, aiding in early and precise diagnosis, thereby facilitating tailored therapeutic interventions for improved patient outcomes.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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Ethics approval

Ethical approval obtained from all patients.

Human and animal rights

This article does not contain any studies with human participants or animals performed by any of the authors.

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