# Differentiating Between Primary Central Nervous System Lymphomas and Glioblastomas: Combined Use of Perfusion-Weighted and Diffusion-Weighted Magnetic Resonance Imaging

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■ OBJECTIVE: **The purpose of this study was to determine whether combined diffusion-weighted imaging and dynamic susceptibility contrast-enhanced perfusion-weighted imaging magnetic resonance imaging can be used to differentiate between common malignant brain tumors, including lymphomas and high-grade gliomas.**

■ METHODS: **We evaluated 87 patients with histologically confirmed brain tumors, including 33 primary central nervous system lymphomas (PCNSLs) and 54 glioblastomas (GBMs). All patients underwent conventional magnetic resonance imaging, diffusion-weighted imaging, and perfusion-weighted imaging before surgical removal of the lesion or stereotactic biopsy.**

■ RESULTS: **The maximum relative cerebral blood volume (rCBV) ratios of GBMs were significantly higher than those of PCNSLs ($P < 0.0001$). The maximum rCBVs helped to distinguish PCNSLs from GBMs with 97.0% sensitivity, 90.7% specificity, and 0.98 area under the curve. The minimum apparent diffusion coefficients (ADCs) of PCNSLs were significantly lower than those of GBMs ($P < 0.0001$). At an rCBV cutoff value of 4.0 and a minimum ADC of $1.0 \times 10^{-3}$ mm$^2$/second, it was possible to differentiate between PCNSLs and GBMs.**

■ CONCLUSIONS: **The combination of rCBV and ADC can facilitate the differentiation between PCNSLs and GBMs.**

## INTRODUCTION

Primary central nervous system lymphomas (PCNSLs) are extranodal malignant lymphomas arising in the brain, spinal cord, leptomeninges, or eyes. At the time of diagnosis, patients are free of lymphomas outside the nervous system. PCNSLs account for less than 5% of all primary central nervous system tumors, and 1%–2% of all lymphomas.[1] Over the last 2 decades, the incidence of PCNSL has reportedly increased.[2-4]

Although PCNSL is invariably fatal without treatment, it is often highly responsive to therapy, and as many as 70% of patients achieve a complete response to initial treatments.[5,6] Current treatments seem to improve the survival of patients with PCNSL; however, disease recurrence and late neurologic toxicity are serious complications.

On contrast-enhanced computed tomography or magnetic resonance imaging (MRI), PCNSLs typically present as uniformly enhancing lesions that are frequently periventricular and can involve the corpus callosum. However, in some cases, it is difficult to distinguish PCNSLs from other central nervous system

**Key words**
- Diagnosis
- Glioblastomas
- Magnetic resonance imaging
- Primary central nervous system lymphoma

**Abbreviations and Acronyms**
**ADC**: Apparent diffusion coefficient
**AUC**: Area under the curve
**CBV**: Cerebral blood volume
**DSC**: Dynamic susceptibility contrast-enhanced
**DWI**: Diffusion-weighted imaging
**FLAIR**: Fluid-attenuated inversion recovery
**FOV**: Field of view
**GBM**: Glioblastoma
**MRI**: Magnetic resonance imaging
**PCNSL**: Primary central nervous system lymphoma
**PWI**: Perfusion-weighted imaging
**rCBV**: Relative cerebral blood volume
**ROC**: Receiver operating characteristic
**ROI**: Region of interest
**TE**: Echo time
**TR**: Repetition time

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disorders, such as glioblastomas (GBMs), metastatic tumors, degenerative diseases, multiple sclerosis, and infectious diseases.[7] Therefore, histologic verification is still required before beginning treatment.

Lymphomas are relatively hyperintense relative to gray matter on diffusion-weighted imaging (DWI) and isointense to hypointense on apparent diffusion coefficient (ADC) maps, consistent with restricted water diffusion.[8-10] In contrast, high-grade gliomas are relatively hyperintense to gray matter on both trace DWIs and ADC maps, consistent with increased diffusivity.[9,11,12] Previous studies have shown statistically significant differences in ADC maps between cerebral lymphomas and GBMs.[8,10] However, restricted water diffusion in GBMs (i.e., hyperintense on trace images and hypointense on ADC maps) has also been reported.[13-17] Therefore, discrimination between lymphomas and some GBMs may be difficult by DWIs only.

Dynamic susceptibility contrast-enhanced (DSC) perfusion-weighted imaging (PWI) MRI has assumed an increasingly important clinical role. It measures T2*-weighted signal intensity decreases occurring dynamically after bolus injections of contrast agent. Signal-time course data analysis provides valuable information, including cerebral blood volume (CBV), which is believed to reflect microvessel density and be useful for differentiating between PCNSLs and GBMs.[18-21]

The aim of this study was to explore the usefulness of PWI and DWI in the differential diagnoses of PCNSLs and GBMs. A 2-step decision tree was used to differentiate between these tumors.

## METHODS

### Patients

All human studies were approved by the review board of the medical ethical committee and were therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Patient consent was waived because of the retrospective nature of this study.

Our study population comprised 87 consecutive patients with histologically confirmed tumors, including 33 PCNSLs and 54 GBMs. All patients underwent conventional MRI, DWI, and PWI before lesion removal or stereotactic biopsy. The mean ages of the patients with PCNSLs and GBMs were 70.5 years (range, 37–86 years) and 69.0 years (range, 12–88 years), respectively. In addition, for the validation study, 6 patients with GBM were included who showed similarity in enhancement pattern to the PCNSLs on conventional MRI (T1-weighted image, T2-weighted image, and T1-weighted image with contrast medium). The mean age of these patients was 77.0 years (range, 38–85 years). The patients with lymphoma had no history of immunosuppression, including infection with the human immunodeficiency virus.

### MRI

MRI was carried out with a 3.0-T scanner (Achieva 3T; Philips Medical Systems, Best, The Netherlands], or MAGNETOM Trio [Siemens, Erlangen, Germany]). Conventional MRI and DWI were carried out during the same procedure. In the examination period, patients were not permitted to use steroids. For conventional MRI, we used a sagittal T1-weighted localizing sequence (repetition time [TR]/echo time [TE] excitations, 15/6/1 milliseconds), and axial T1-weighted (TR/TE excitations, 670/14/1 milliseconds), fast spin-echo T2-weighted (TR/TE [effective] excitations, 3500/96/2 milliseconds; echo train length, 7), and fluid-attenuated inversion recovery (FLAIR; TR/TE [effective]/inversion time, 6000/120/2000 milliseconds; echo train length, 17) sequences, and a triplanar contrast-enhanced T1-weighted sequence. In contrast-enhanced studies, we administered gadopentetate dimeglumine (Magnevist [Bayer Schering, Osaka, Japan]) at a rate of 0.1 mmol/kg body weight. The T1-weighted, T2-weighted, and FLAIR sequences were acquired at a section thickness of 5 mm, with an intersection gap of 1 mm, a matrix of 256 × 512, and a field of view (FOV) of 220 mm.

DWI was performed in the transverse plane using a spin-echo planar imaging sequence according to the following parameters: TR/TE inversion time of 3246/63/1 milliseconds at 3.0 T (Philips) and 3600/81/3 milliseconds at 3.0 T (Siemens); diffusion gradient encoding in 3 orthogonal directions; b = 1000 seconds/mm$^2$; FOV, 23 × 23 cm (Philips and Siemens); matrix size, 128 × 128 pixels (Siemens) or 192 × 192 pixels (Philips); section thickness, 5 mm; section gap, 1 mm; number of signals acquired, 1. DWI was performed before contrast-enhanced T1-weighted imaging.

ADC values were calculated as follows: ADC = −[ln(*Sb*/*So*)]/b; where *Sb* is the signal intensity of the region of interest (ROI) obtained from 3 orthogonally oriented DWIs or diffusion trace images, *So* is the signal intensity of the ROI acquired via reference T2-weighted images, and b is the gradient b factor with a value of 1000 seconds/mm$^2$. ADC maps were calculated on a pixel-by-pixel basis.

A preloading dose of gadopentetate dimeglumine (Magnevist, 0.06 mmol/kg of body weight) was injected before each DSC scan to correct for T1-weighted leakage effects that lead to TBE underestimation. DSC perfusion MRI was performed during injection of a bolus of gadopentetate dimeglumine (Magnevist, 0.07 mmol/kg body weight) at a rate of 3 mL/second through a 20-gauge intravenous catheter, immediately followed by a bolus injection of saline (3 mL/second; total, 20 mL).

DSC perfusion MRI scans were acquired with a single-shot gradient-echo planar imaging sequence (TR/TE, 1400/32 milliseconds; flip angle, 60°; FOV, 23 cm; matrix, 128 × 128; section thickness/gap, 5/1 mm; in-plane resolution, 1.8 × 1.8 mm; acquisition time, 1 minute 17 seconds). A total of 50 dynamic series of 19 sections, to cover the entire brain, were obtained. Subsequently, transverse T1-weighted (TR/TE, 600/8.5 milliseconds) and magnetization-prepared rapid acquisition of gradient echo (TR/TE, 1900/4.7 milliseconds; TI, 900 seconds) sequences were performed. To analyze relative cerebral blood volume (rCRV) from DSC perfusion MRI data, we used commercially available built-in software (Siemens). For DSC perfusion MRI, arterial input functions were manually defined by 1 radiologist and 1 technologist by selecting 10–16 pixels containing the M1 or M2 segment of the middle cerebral artery in the sylvian fissure. Each pixel was confirmed to contain the middle cerebral artery by anatomic location and a susceptibility time curve, showing a steeper slope and greater amplitude than in the adjacent brain parenchyma.

### Image Analysis

To assess the brain tumors based on imaging, surgical, and histologic data, we evaluated the entire series of MRI scans on a