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QUANTITATIVE MORPHOMETRIC ALTERATIONS OF PERICELLULAR AND PERIVASCULAR SPACES AS HISTOLOGICAL CORRELATES OF MRI SIGNAL CHANGES IN BRAIN TUMORS: A CLINICOPATHOLOGICAL STUDY OF 273 CASES

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Introduction

Brain tumors remain one of the most diagnostically challenging entities in neuro-oncology. Despite remarkable advances in MRI technology, the histological basis of specific MRI signal characteristics — particularly T2/FLAIR hyperintensity and contrast enhancement patterns — is incompletely understood at the quantitative morphometric level. While sensitivity and specificity of MRI for brain tumor detection are well-documented, systematic correlation between MRI semiotics and quantitative tissue architecture parameters, such as pericellular space (PCS) and perivascular space (PVS), has not been established in the Central Asian patient population.

The present study addresses this gap by quantifying PCS and PVS across histologically verified brain tumor subtypes and determining their correlation with preoperative MRI findings, thereby providing a morphological substrate for MRI signal interpretation.

Materials and Methods

A retrospective clinicopathological study was conducted on 273 consecutive patients who underwent surgical resection of brain tumors between 2021 and 2024. Tumors were classified according to WHO Classification of Central Nervous System Tumors 2021 into benign (n=212, 77.7%) and malignant (n=61, 22.3%) groups.

Preoperative MRI was performed on a 1.5T scanner using a standard protocol (T1-WI, T2-WI, FLAIR, gadolinium-enhanced T1). Assessed parameters included: signal intensity characteristics, structural homogeneity, contrast enhancement pattern (ring vs. homogeneous), presence of necrotic areas, and degree of perifocal edema.

Histopathological analysis was performed on hematoxylin-eosin stained sections at ×400 magnification (objective ×40, ocular ×10). Morphometric assessment was performed on 10 standardized visual fields per specimen (field area: 0.0625 mm²) using an ocular micrometer in a blinded manner. PCS and PVS were expressed as percentage of total visual field area. Statistical analysis included Spearman rank correlation (rs), chi-square test, Student's t-test, positive predictive value (PPV), and negative predictive value (NPV) using SPSS v26.0. Significance threshold: $p<0.05$.

Patient Characteristics

Tumor type	n	n (%)	Mean age (yr)	F/M ratio (%)
Meningioma	80	29.3%	48±5.2	60/40
Astrocytoma (II)	49	17.9%	44±4.8	45/55
Pituitary adenoma	35	12.8%	42±5.0	54/46
Oligodendroglioma	21	7.7%	39±6.1	43/57

Ependymoma	7	2.6%	53±3.0	43/57
Glioblastoma (IV)	22	8.1%	52±6.3	40/60
Anaplastic astrocytoma (III)	39	14.3%	46±5.4	45/55
Metastatic tumors	8	2.9%	56±4.0	75/25
Meningiosarcoma	7	2.6%	50±5.1	57/43
Other malignant	5	1.8%	49±3.8	40/60
TOTAL	**273**	**100%**	**47.2±5.3**	**51/49**

Results

Benign and malignant tumors demonstrated statistically significant differences across all MRI parameters ($p<0.001$). Ring-like contrast enhancement was present in 80.3% of malignant vs. 5.2% of benign tumors. Suspected necrotic areas on MRI were found in 78.7% of malignant vs. 8.0% of benign cases ($\chi^2=124.6$, $p<0.001$; 9.8-fold excess in malignant group). T2 heterogeneous signal was exclusively observed in malignant tumors (72.1% vs. 0%, $p<0.001$). Severe perifocal edema (+++) was present in 85.2% of malignant vs. 9.9% of benign tumors.

Morphometric analysis revealed significantly lower PCS values in malignant tumors (3.3±0.40%) compared to benign tumors (3.7±0.24%, $p<0.05$). The highest PCS values were recorded in oligodendroglioma (4.5±0.22%) and ependymoma (4.2±0.30%), reflecting preserved stromal architecture. PVS was quantifiable in astrocytoma (4.9±0.15%) and ependymoma (3.7±0.33%), where T2/FLAIR hyperintensity correlated directly with PCS/PVS enlargement ($rs=+0.84$, $p<0.001$).

MRI parameter	Morphological correlate	rs	Strength
T2/FLAIR perifocal hyperintensity	PCS/PVS enlargement	+0.84*	Strong
T2 heterogeneous signal	Necrosis + hemorrhage	+0.91*	Strong
MRI suspected necrosis	Histological necrosis	+0.95*	Very strong
Contrast enhancement intensity	Endothelial proliferation	+0.86*	Strong

*$p<0.001$ for all correlations.

The combined MRI algorithm demonstrated the following diagnostic performance: for benign tumors (homogeneous contrast + well-defined margins + homogeneous structure + absent/mild edema) — sensitivity 95.6%, specificity 96.8%, PPV 94.2%, NPV 97.4%, accuracy 96.3%; for malignant tumors (ring contrast + necrosis + severe edema) — sensitivity 91.8%, specificity 94.3%, PPV 82.4%, NPV 97.6%, accuracy 93.8% (all $p<0.001$).

Glioblastoma (n=22) exhibited the most pathognomonic MRI profile: ring contrast enhancement (100%), suspected central necrosis (95.5%), T2 heterogeneous signal (90.9%), severe perifocal edema (100%), and hemorrhagic foci (63.6%). The combination of all five features predicted glioblastoma with 98.2% confidence. Metastatic tumors characteristically presented with multiple foci (62.5%) and subcortical (grey-white matter junction) localization (75%).

Discussion

The very strong correlation between MRI-suspected necrosis and histologically confirmed necrosis ($rs=+0.95$) provides robust quantitative support for the clinical use of MRI as a surrogate for tissue necrosis assessment. The reduction in PCS (3.7±0.24% vs. 3.3±0.40%) and PVS in malignant tumors likely reflects progressive cellular crowding,

vascular remodeling, and peritumoral compression secondary to rapid infiltrative growth. The strong correlation between T2/FLAIR hyperintensity and PCS/PVS enlargement (rs=+0.84) confirms that interstitial fluid accumulation in perivascular and pericellular compartments is the primary morphological substrate of T2 signal elevation in low-grade tumors.

These findings are consistent with the neurovascular unit disruption model, in which pericellular and perivascular compartments serve as the earliest indicators of microstructural tissue remodeling in both benign and malignant neoplasms, preceding macroscopic edema visible on conventional MRI.

Conclusions

(1) MRI semiotics demonstrates high concordance with pathomorphological findings across all brain tumor types, enabling preoperative malignancy prediction with 93.8% accuracy. (2) Quantitative morphometric assessment of PCS (3.7±0.24% benign vs. 3.3±0.40% malignant) provides an objective histological parameter for tumor differentiation. (3) The very strong MRI-necrosis correlation (rs=+0.95) validates MRI as a reliable non-invasive surrogate for tissue necrosis. (4) Integration of morphometric parameters with MRI data enhances diagnostic precision and should be incorporated into routine neuropathological reporting protocols.