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Determination of sensitivity and specificity of Magnetic Resonance Spectroscopy (MRS) in evaluation of rim enhancing brain lesions

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ABSTRACT

Background: *Rim-enhancing brain lesions present a diagnostic challenge due to overlapping imaging features between neoplastic and non-neoplastic pathologies. Accurate preoperative differentiation is crucial for appropriate management. This study aimed to determine the sensitivity and specificity of Magnetic Resonance Spectroscopy (MRS) in differentiating high-grade gliomas from cerebral abscesses, using histopathology as the reference standard.* ***Methods & Materials:*** *A cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from July 2022 to June 2023. Twenty-nine patients with suspected rim-enhancing brain lesions underwent conventional MRI and single-voxel proton MRS. Metabolites including N-acetylaspartate (NAA), choline (Cho), creatine (Cr), and lactate were analyzed. Histopathological examination of surgical specimens served as the gold standard. Diagnostic performance of MRS was evaluated using sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV).* ***Results:*** *The mean age of participants was 41.23 ± 15.07 years, with a male predominance (55.2%). Headache, nausea, vomiting, and seizures were the most common presenting symptoms. High-grade gliomas constituted 51.7% and cerebral abscesses 48.3% of MRS diagnoses. MRS demonstrated elevated Cho/Cr ratios in gliomas (2.94 ± 1.83) and higher NAA/Cr ratios in abscesses (1.89 ± 0.69), both statistically significant ($p < 0.05$). Sensitivity, specificity, and accuracy of MRS were 100%, 82.2%, and 93.1% for cerebral abscesses, and 100% for all parameters in high-grade gliomas.* ***Conclusion:*** *MRS is a reliable, non-invasive adjunct to conventional MRI for differentiating rim-enhancing brain lesions, with excellent diagnostic accuracy. Incorporation of metabolite ratios enhances lesion characterization and guides clinical decision-making. Further multicenter studies with larger cohorts are recommended.*

Keywords: *Rim-enhancing brain lesions, Magnetic Resonance Spectroscopy (MRS), High-grade glioma, Cerebral abscess, Diagnostic accuracy, Cho/Cr ratio, NAA/Cr ratio.*

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INTRODUCTION

Rim-enhancing intracranial lesions are a common diagnostic challenge, as both neoplastic and non-neoplastic pathologies may present with similar imaging features on conventional CT and MRI [1]. Such lesions may represent cerebral abscesses, gliomas, metastases, or other infectious and inflammatory conditions, making accurate preoperative diagnosis essential for appropriate management [1,2].

Conventional MRI is sensitive in detecting these lesions but lacks specificity in differentiating tumors from infections, leading to potential misclassification [3]. High-grade gliomas typically show necrosis, hypoxia, and blood–brain barrier disruption, while cerebral abscesses exhibit central liquefaction; however, both appear as rim-enhancing lesions, often mimicking one another [4]. Hence, additional diagnostic tools are needed.

Proton Magnetic Resonance Spectroscopy (MRS) provides metabolic information by quantifying brain metabolites such as N-acetylaspartate (NAA), choline (Cho), creatine (Cr), and lactate [5,6]. Characteristic metabolic patterns, including decreased NAA, elevated Cho, and presence of lactate and lipids, assist in differentiating gliomas from abscesses [5]. Previous studies have demonstrated that MRS significantly improves diagnostic accuracy when combined with conventional MRI [7,8].

Few studies in Bangladesh have systematically evaluated the diagnostic performance of MRS compared with histopathology. Given the overlapping radiological appearances of rim-enhancing brain lesions and the need for early, accurate diagnosis in guiding treatment, this study aims to evaluate the sensitivity and specificity of MRS in differentiating high-grade gliomas from cerebral abscesses, using histopathology as the gold standard in a Bangladeshi population.

METHODS & MATERIALS

Study Setting and Duration

This cross-sectional study was carried out in the Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka medical College, Dhaka, Bangladesh, over a period of one year from July 2022 to June 2023.

Study Population

The study population comprised patients with brain lesions referred to the Department of Radiology and Imaging from various surgical and medical departments of BSMMU for MRS examination.

Sampling Method and Sample Size

Purposive sampling was used to select study participants. The sample size was calculated using power analysis for a single

proportion [9]. We hypothesized that the sensitivity of MRS in the diagnosis of rim-enhancing brain lesions would be ≥95%. Using a power level of 80% (Z_β = 0.84) and a 5% α error (Z_α = 1.96, two-tailed), and considering a sensitivity of 84% reported by Zeng et al. [10], the estimated sample size was 29.

Selection Criteria

Inclusion Criteria: Patients from indoor, outdoor, and emergency units with suspected brain lesions referred for MRS examination.

Exclusion Criteria: Patients with contraindications to MRI, including those with cardiac pacemakers, prosthetic heart valves, cochlear implants, or brain aneurysm clips, were excluded from the study. Additionally, patients with recurrent or metastatic tumors, cystic or necrotic regions, or jerky movements that could interfere with imaging were not included. Those in whom MRS or histopathological examination was not feasible, as well as uncooperative patients or individuals who did not provide informed consent, were also excluded.

Outcome Variables

A) Demographic and Clinical Variables: Age, sex, headache, hemiparesis, blurring of vision, nausea and vomiting, fever

B) MRS Variables: Choline (Cho), Creatine (Cr), Cho/Cr ratio, N-acetylaspartate (NAA), NAA/Cr ratio

Study Procedure

After obtaining informed consent, clinical data were collected using a pre-tested structured questionnaire. Surgical intervention was performed for all patients, and the histopathological findings were compared with MRS results to evaluate diagnostic concordance.

Magnetic Resonance Spectroscopy (MRS) Protocol

Proton MRS was performed using a single-voxel technique with a point-resolved spectroscopy sequence (TR/TE/NEX: 2000/136 ms/128; voxel size: 20×20×20 mm). The voxel was placed at the center of the lesion, avoiding cystic or necrotic areas, based on pre-contrast spin echo MR images, in consensus with two radiologists. The relatively long echo time minimized baseline distortions and simplified spectra to the four primary metabolites of interest. The scan duration for each spectral acquisition was approximately 4 minutes.

Histopathological Evaluation

Tissue specimens obtained during surgery were formalin-fixed, paraffin-embedded, and evaluated by light microscopy using hematoxylin and eosin staining. Histopathology reports were collected from the pathology department and correlated with MRS findings.

Research Instruments

A) Pre-tested structured questionnaire for clinical and demographic data collection.
B) Magnetic Resonance Spectroscopy (MRS) machine for metabolite analysis.

Statistical Analysis

Data were analyzed using SPSS version 22. Descriptive statistics were presented as frequency, percentage, mean, and standard deviation. The diagnostic performance of MRS was assessed by calculating sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV). Comparisons between metabolite ratios were performed using the unpaired t-test, with a p-value <0.05 considered statistically significant. Results were presented in tables, figures, and diagrams.

Ethical Considerations

The study protocol was approved by the local ethics committee. The objectives, procedures, alternatives, risks, and benefits were explained to participants in a language they could understand. Written informed consent was obtained from all patients. Confidentiality of patient data was maintained throughout the study, and participation did not affect routine medical care.

RESULTS

It was observed that the majority (41.4%) of patients belonged to the age group 41–60 years, with a mean age of 41.23 ± 15.07 years (range: 5–73 years). More than half (55.2%) of the patients were male and the male-to-female ratio was approximately 1.3:1. Regarding clinical presentation, the most common symptom was headache (86.2%), followed by nausea and vomiting (69.0%) and seizure (58.6%). Other reported symptoms included hemiparesis (48.3%), blurring of vision (34.5%), and fever (31.0%). Based on MRS diagnosis, slightly more than half (51.7%) of the patients had high-grade glioma, while 48.3% were diagnosed with cerebral abscess. *Table I* shows the demographic, clinical, and MRS diagnostic characteristics of the study patients.

Table I: Distribution of the study patients by demographic, clinical, and MRS diagnosis variables (*n* = 29)

Variable	Category	Number of Patients	Percentage (%)
Age (in years)	0 – 20	10	34.4
	21 – 40	4	13.8
	41 – 60	12	41.4
	61 – 80	3	10.4
	Mean ± SD	41.23 ± 15.07	
	Range (min–max)	5 – 73	
Sex	Male	16	55.2
	Female	13	44.8
Clinical Presentation	Headache	25	86.2
	Nausea & vomiting	20	69.0
	Seizure	17	58.6
	Hemiparesis	14	48.3
	Blurring of vision	10	34.5
	Fever	9	31.0
MRS Diagnosis	High grade glioma	15	51.7
	Cerebral abscess	14	48.3

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Table II shows by MRI findings by study patients, it was observed that half (50.0%) patients belonged to size of lesion 3.1-6.5 (cm) in cerebral abscess and 11(74.4%) in high grade glioma, 14(100.0%) patients had T1 Hypointense in cerebral abscess and 13(86.7%) in high grade glioma, 14(100.0%) patients had T2 Hyperintense in cerebral abscess and similarly in high grade glioma, 14(100.0%) patients had FLAIR Hyperintense in cerebral abscess and similarly in high grade glioma, 12(85.7%) patients had peritumoral oedema in cerebral abscess and 15(100.0) in high grade Glioma, 12(85.7%) patients had mass effect in cerebral abscess and 15(100.0) in high grade Glioma, 7(50.0%) patients had moderate enhancement on T_1 in cerebral abscess and 3(20.0) in high grade Glioma, 14(100.0%) patients had nature of enhancement ring in cerebral abscess and 15(100.0) in high grade Glioma, 12(85.7%) patients had area of necrosis in cerebral abscess and 13(86.7) in high grade Glioma 1(7.1%) patients had area of hemorrhage in cerebral abscess and 5(33.3) in high grade Glioma.

Table II: Distribution of the study patients by MRI findings (*n*=29)

MRI findings	Cerebral Abscess (n=14)	High Grade Glioma (n=15)
	Number of patients (%)	Number of patients (%)
Size of lesion (cm)		
0.5-0.9	3(21.4)	2(13.3)
1-3	4(28.6)	2(13.3)
3.1-6.5	7(50.0)	11(74.4)
T1		
Hypointense	14(100.0)	13(86.7)
Hyperintense	0(0.0)	2(13.3)
T2		
Hypointense	0(0.0)	0(0.0)
Hyperintense	14(100.0)	15(100.0)
FLAIR		
Hypointense	0(0.0)	0(0.0)
Hyperintense	14(100.0)	15(100.0)
Peritumoral oedema		
Present	12(85.7)	15(100.0)
Absent	2(14.3)	0(0.0)
Mass effect		
Present	12(85.7)	15(100.0)
Absent	2(14.3)	0(0.0)
Enhancement on T1		
Mild	0(0.0)	0(0.0)
Moderate	7(50.0)	3(20.0)
Intense	7(50.0)	12(80.0)
Non Enhanced	0(0.0)	0(0.0)
Nature of Enhancement		
Ring	14(100.0)	15(100.0)
Non – Ring	0(0.0)	0(0.0)
Area of Necrosis		
Present	12(85.7)	13(86.7)
Absent	2(14.3)	2(13.3)
Area of Hemorrhage		
Present	1(7.1)	5(33.3)
Absent	13(92.9)	10(66.7)

Cerebral abscess showed a minor decrease in NAA, Cho, Cho/Cr, and NAA/Cr, with a minor increase in lactate. In contrast, high-grade glioma exhibited a minor decrease in NAA and NAA/Cr, with a marked increase in Cho, lactate, and Cho/Cr. Quantitative analysis revealed that the mean Cho/Cr ratio was significantly higher in high-grade glioma (2.94 ± 1.83) compared to cerebral abscess (0.95 ± 0.17), and the mean NAA/Cr ratio was significantly lower in glioma (0.72 ± 0.35) compared to abscess (1.89 ± 0.69). Both differences were statistically significant ($p < 0.05$) *Table III*.

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Table III: Semiquantitative assessment and quantitative metabolite ratios in cerebral abscess and high-grade glioma (*n* = 29)

Metabolite / Ratio	Cerebral Abscess (n=14)	High Grade Glioma (n=15)	p-value
NAA	Minor ↓	Minor ↓	–
Cho	Minor ↓	↑	–
Lac	Minor ↑	↑	–
Cho/Cr	Minor ↓ 0.95 ± 0.17 Median 0.84 (0.32–2.03)	↑ 2.94 ± 1.83 Median 2.37 (0.91–10.12)	0.002 s
NAA/Cr	Minor ↓ 1.89 ± 0.69 Median 1.72 (0.56–3.43)	Minor ↓ 0.72 ± 0.35 Median 0.62 (0.12–2.02)	0.049 s

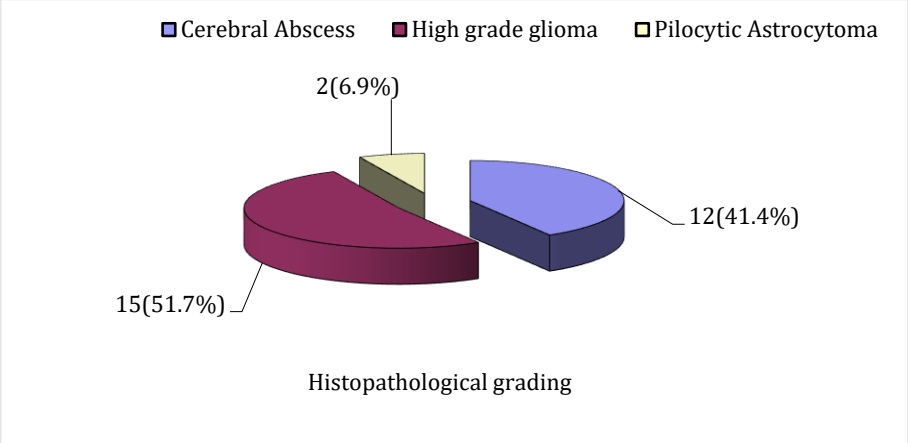

Figure 1: Pie chart shows histopathological grading of the study patients

All patients in this study underwent operative intervention. Histopathological analysis revealed that more than half of the patients (51.7%) were diagnosed with high-grade glioma, followed by cerebral abscess in 41.4% of cases, and pilocytic astrocytoma in 6.9% of cases (*Figure 1*). These findings indicate that the majority of rim-enhancing brain lesions were neoplastic in origin, with high-grade glioma being the most frequent histopathological outcome.

Table IV shows the diagnostic performance of MRS compared with histopathological findings in cerebral abscess and high-grade glioma. For cerebral abscess, MRS correctly identified 12 true positive cases and 15 true negatives, with 2 false positives and no false negatives. For high-grade glioma, MRS correctly identified all 15 true positives and 14 true negatives, without any false positive or false negative cases. These findings indicate that MRS demonstrated excellent diagnostic accuracy for high-grade glioma, and very good accuracy for cerebral abscess, with only a small number of false positive results.

Table IV: Comparison of MRS with histopathological findings of cerebral abscess and high-grade glioma (*n* = 29)

MRS Diagnosis	Histopathology +ve	Histopathology –ve	Total
Cerebral Abscess +ve	12 (True Positive)	2 (False Positive)	14
Cerebral Abscess –ve	0 (False Negative)	15 (True Negative)	15
Total (Abscess)	12	17	29
High Grade Glioma +ve	15 (True Positive)	0 (False Positive)	15
High Grade Glioma –ve	0 (False Negative)	14 (True Negative)	14
Total (Glioma)	15	14	29

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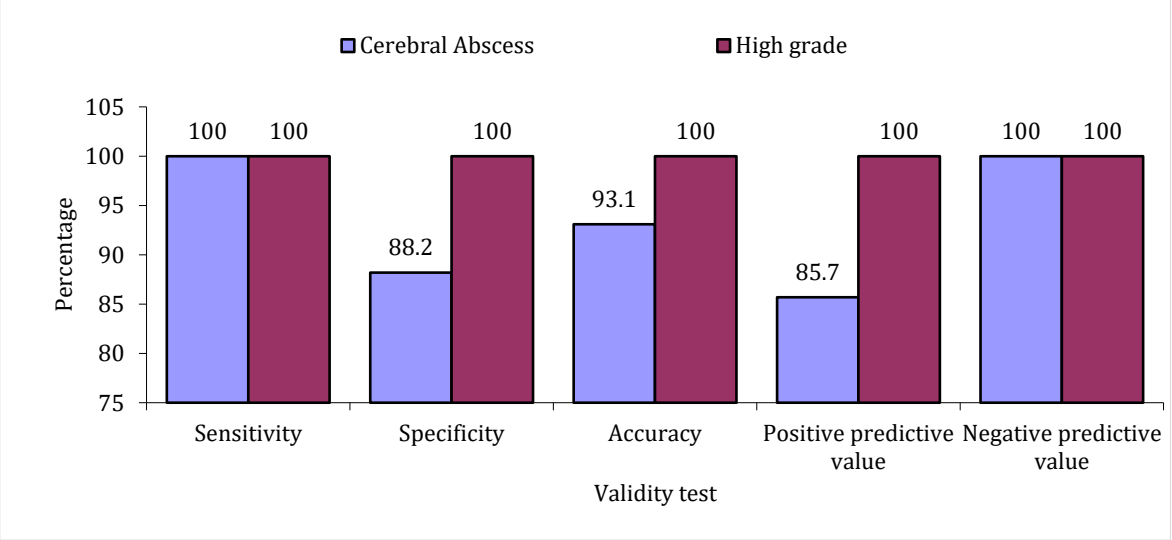

Figure 2: Bar diagram showing Validity test of MRS with histopathological finding of Rim Enhancing lesions

Figure 2 shows validity test of MRS finding with histopathological diagnoses of rim enhancing lesions of the study patients. It was observed that, patients were correlated by calculating sensitivity, specificity, accuracy, positive and negative predictive values.

DISCUSSION

Clinical Challenge of Rim-Enhancing Brain Lesions

Evaluation of rim-enhancing intracranial lesions represents a significant diagnostic challenge for clinicians and radiologists. Non-invasive diagnosis often relies on clinical history and conventional radiological imaging, which can provide an initial diagnostic orientation. However, histopathological examination is frequently required to establish a definitive diagnosis, especially before initiating aggressive treatments. Even in cases where surgery is not the primary treatment, additional non-invasive diagnostic information is valuable in guiding clinical decision-making and potentially reducing the need for surgical interventions. Proton Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique that measures the biochemical composition of living tissues, providing metabolic information that complements anatomical imaging and assists in the evaluation of various brain diseases.

Study Population and Demographics

This cross-sectional study included 29 patients with rim-enhancing brain. The mean age of participants was 41.23 ± 15.07 years (range 5–75 years), with the highest proportion of patients (34.5%) in the 41–50 years age group. This is consistent with Zeng et al. [10], who reported a mean age of 44.92 ± 12.65 years, and with Bava et al. [11], whose series included patients aged 2–75 years. The majority of participants were male (55.2%), with a male-to-female ratio of 1.3:1, comparable to findings reported by Bava et al. [11] and Dhar et al. [12].

Clinical Presentation

Headache was the most common presenting symptom (86.2%), followed by nausea and vomiting (69.0%), seizures (58.6%), hemiparesis (48.3%), blurring of vision (34.5%), and fever (31.0%). These findings align with previous studies, including Taylor [13], who reported headaches in 50% of patients with intracranial lesions, and Elsadway et al. [14], who reported visual disturbances, limb weakness, and altered consciousness among patients with ring-enhancing lesions.

Imaging Findings

Magnetic resonance imaging (MRI) characteristics showed that most lesions measured 3.1–6.5 cm, reflecting delayed presentation often seen in lower socio-economic populations. Liberman et al. [15] found that the frequency of malignancy increased significantly with lesion size. Cerebral abscesses predominantly showed T1 hypointensity (100%), while 86.7% of high-grade gliomas were T1 hypointense, and 13.3% displayed T1 hyperintensity, likely due to hemorrhage. All lesions were hyperintense on T2 and FLAIR sequences, highlighting the nonspecific nature of conventional MRI in differentiating tumor from abscess. Chung et al. [16] reported that high signal intensity on T2-weighted images, lesion diameter greater than 30 mm, and heterogeneous signal intensity on T1-weighted MR images predicted malignancy with the highest sensitivity, while Elsadway et al. [14] observed similar diagnostic ambiguity when classifying and evaluating ring-enhancing lesions using MRI alone in a series of 25 patients.

Peritumoral edema was present in 85.7% of abscesses and 100% of high-grade gliomas, with corresponding mass effect in 85.7% and 100%, respectively. These results are comparable to Dean et al. [17], who emphasized mass effect and necrosis as critical predictors of tumor grade.

Contrast enhancement was predominantly intense in high-grade gliomas (80%) and cerebral abscesses (50%), with ring enhancement observed in all lesions, reflecting the inclusion criteria of the study. Necrosis was present in 86.7% of cerebral abscesses and high-grade gliomas, consistent with Fan [18], who emphasized necrosis as a distinguishing feature in glioma grading.

MRS Findings

Semiquantitative analysis of MRS demonstrated minor decreases in NAA, Cho, Cho/Cr, and NAA/Cr in cerebral abscesses, with a minor increase in lactate. In high-grade gliomas, there was a minor decrease in NAA and NAA/Cr, accompanied by marked increases in Cho, Cho/Cr, and lactate. The mean Cho/Cr ratio was significantly higher in high-grade gliomas (2.94 ± 1.83) compared to cerebral abscesses (0.95 ± 0.17), while the mean NAA/Cr ratio was significantly lower in

gliomas (0.72 ± 0.35) compared to abscesses (1.89 ± 0.69), consistent with previous study [19].

Histopathological Correlation and Diagnostic Accuracy

All patients underwent surgical intervention. Histopathology revealed that 51.7% had high-grade gliomas, 41.4% had cerebral abscesses, and 6.9% had pilocytic astrocytomas. MRS showed excellent concordance with histopathological findings: for cerebral abscesses, there were 12 true positives, 2 false positives, 0 false negatives, and 15 true negatives; for high-grade gliomas, all cases were correctly identified.

The diagnostic performance of MRS, using histopathology as the gold standard, demonstrated sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) of 100%, 82.2%, 93.1%, 85.7%, and 100% for cerebral abscesses, respectively. For high-grade gliomas, all parameters were 100%. These results are consistent with prior studies [20-22], which reported high sensitivity and specificity of MRS in differentiating abscess from necrotic tumors.

CONCLUSION & RECOMMENDATIONS

This study assessed the diagnostic performance of Magnetic Resonance Spectroscopy (MRS) in differentiating rim-enhancing brain lesions. Among 29 patients, rim-enhancing lesions were most frequent in the fifth decade of life, with a male predominance. The common presenting symptoms included headache, nausea and vomiting, and seizures. Lesion size of 1–3 cm predominated in cerebral abscesses, while lesions of 3.1–6.5 cm were more frequent in high-grade gliomas. On conventional MRI, hypointensity on T1 and hyperintensity on T2 and FLAIR were observed in both groups, with peritumoral edema and mass effect more pronounced in high-grade gliomas. Enhancement patterns varied, with cerebral abscesses showing mild to moderate homogeneous enhancement and high-grade gliomas demonstrating moderate, heterogeneous, or ring-pattern enhancement. Semiquantitative MRS analysis revealed increased Cho/Cr in high-grade gliomas and elevated NAA/Cr in cerebral abscesses. Histopathological findings showed strong concordance with MRS, and validity tests indicated high sensitivity, specificity, and accuracy.

These findings support the use of MRS as a reliable, non-invasive adjunct to conventional MRI for preoperative evaluation and differentiation of rim-enhancing brain lesions. Quantitative measures, including choline levels and Cho/Cr ratio, may aid in lesion characterization and grading. Future multicenter studies with larger sample sizes are recommended, incorporating additional metabolites such as lipid and myoinositol, to further enhance the diagnostic utility of MRS and guide patient management more effectively.

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