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Role of magnetic resonance spectroscopy, diffusion-weighted imaging, and apparent diffusion coefficient in distinguishing intracranial space-occupying lesions.

Parth Bhayana[1], Neekita Meher[2*], Santosh Kumar Padhy[3], Pravakar Bahinipati[4]

[1]Senior Resident, Department of Radiodiagnosis, Institute of Medical Sciences and SUM Hospital, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha, India.

[2]Assistant Professor, Department of Radiodiagnosis, Institute of Medical Sciences and SUM Hospital, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha, India.

[3]Associate Professor, Department of Radiodiagnosis, Institute of Medical Sciences and SUM Hospital, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha, India.

[4]Professor, Department of Radiodiagnosis, Institute of Medical Sciences and SUM Hospital, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha, India.

Abstract

Introduction

Objectives: To evaluate the role of magnetic resonance spectroscopy (MRS), diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) mapping in distinguishing infective from neoplastic intracranial space-occupying lesions (ICSOLs).

Methods

This prospective observational study was conducted at a tertiary care teaching hospital over two years. Eighty patients presenting with seizures, headache, neurological deficits, or an intracranial space-occupying lesion detected on computed tomography underwent multiparametric MRI, including conventional MRI, DWI, ADC mapping, and MRS. Imaging findings were correlated with histopathological diagnoses. Statistical analyses were performed using appropriate parametric and non-parametric tests, with a p-value <0.05 considered statistically significant.

Results

The mean age of the participants was **49.0 ± 16.8 years**, with an equal gender distribution (50% males and 50% females). Peri-lesional ADC values were significantly higher than intra-lesional ADC values across all lesion groups, particularly in high-grade tumours (1.57 ± 0.14 vs. $0.87 \pm 0.23 \times 10^{-3}$ mm²/s; **$p < 0.001$**). Diffusion restriction patterns showed significant associations with tumour grade and lesion etiology. Spectroscopic analysis demonstrated significantly lower absolute choline levels in high-grade malignancies than in benign lesions (**$p = 0.013$**), while benign extra-axial lesions exhibited the highest Cho/NAA ratio (8.47 ± 2.25).

Conclusion

Multiparametric MRI substantially improves the characterization of ICSOLs by integrating anatomical, diffusion, and metabolic information. Combined interpretation of conventional MRI, DWI, ADC mapping, and MRS enhances diagnostic confidence and facilitates accurate preoperative lesion characterization and grading.

Recommendation

Multiparametric MRI should be incorporated into the routine preoperative evaluation of patients with suspected ICSOLs whenever available. Larger multicenter studies are recommended to validate these findings and establish standardized imaging protocols for differentiating infective and neoplastic lesions.

Keywords: *Magnetic Resonance Spectroscopy; Diffusion-Weighted Imaging; Apparent Diffusion Coefficient; Intracranial Space-Occupying Lesions; Glioblastoma.*

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Corresponding author: *Neekita Meher[*]*

Email: ***neekita.22@gmail.com***

Assistant Professor, Department of Radiodiagnosis, Institute of Medical Sciences and SUM Hospital, Siksha O Anusandhan Deemed to be University, Bhubaneswar, Odisha, India

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Introduction

Louis initially described a tumour and a fungus of the dura mater in 1774, marking the beginning of the discovery of space-occupying diseases in the cerebral cavity (1). In terms of cause, intracranial space-occupying lesions (ICSOLs) can be classified into two types: neoplastic and non-neoplastic (caused by inflammation and/or infection). When examining ICSOLs in a clinical environment, a precise identification of neoplastic origin is crucial for prompt neurosurgical intervention (2). For the diagnosis of CNS malignancies, contrast-enhanced CT (CECT) and magnetic resonance imaging (MRI) are often used (3,4). CT is a helpful technique for evaluating clinically unstable patients and is more effective than MRI for evaluating hyperacute haemorrhages, calcifications, and skull lesions. In post-treatment imaging, SPECT and PET scans are far more useful for detecting tumour recurrence than for detecting radiation-induced necrosis. Biopsies are still the primary method of diagnostic confirmation, nevertheless. Needle biopsies are essential before or during surgery, except when radiologic and clinical findings suggest a benign tumour that can be managed with active monitoring. Magnetic resonance spectroscopy (MRS) is a new, improved imaging method that provides supplemental, noninvasive information about the biochemical composition of tissues (3,5). It is an addition to MRI, a type of imaging technology [6].

MRS offers a non-invasive window into the body's metabolic functions. Applications in clinical practice are becoming more widespread; thus, their use is no longer limited to research. Recent improvements in whole-body MRI enable the acquisition of clinical MRS after a standard MRI, thereby combining functional data with anatomical information (7). Diffusion-weighted imaging (DWI) is a method that generates signal contrast by exploiting differences in Brownian motion. A method known as DWI is used to evaluate the microarchitecture and molecular function of the human body. The DWI signal contrast may be assessed using apparent diffusion coefficient (ADC) maps, a technique that can be used to evaluate the response to therapy and the progression of the disease (8).

MR imaging methods like DWI and MR spectroscopy may improve the precision of these tumour diagnoses. The ability of MR sequences to differentiate between low-grade and high-grade malignancies helps doctors plan treatments and evaluate prognoses (9). More precise and effective methods for diagnosing and describing ICSOLs across all age groups are still needed, despite advances in imaging techniques. This research is interesting since it examines how well MRS, DWI, and ADC work together to evaluate ICSOLs in all age groups. This method may provide important new insights into the challenges of diagnosing and treating ICSOLs in diverse populations. This research examines the synergistic role of MRS, DWI, and ADC in distinguishing and diagnosing intracranial lesions across all age groups, aiming to enhance clinical outcomes and diagnostic accuracy. Precise preoperative characterization of intracranial space-occupying lesions (ICSOLs) is crucial for guiding neurosurgical intervention and formulating therapeutic strategies.

Methods

Study design

This was a **prospective observational study** conducted to evaluate the role of multiparametric magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping, and magnetic resonance spectroscopy (MRS), in differentiating infective from neoplastic intracranial space-occupying lesions (ICSOLs), using histopathological diagnosis as the reference standard.

Study setting

The study was conducted in the **Department of Radiodiagnosis, [Hospital Name]**, a tertiary care teaching hospital in **[City, State, India]**. The hospital provides comprehensive diagnostic and therapeutic services, including emergency care, neurology, neurosurgery, oncology, intensive care, advanced neuroimaging, and histopathology facilities. It serves as a major referral center for patients with neurological disorders from urban and rural regions.

The study was carried out over two years **from January 2023 to December 2024**.

Participants

Inclusion criteria

Patients were eligible for inclusion if they:

- were aged **18 years or older**;
- presented with seizures, headache, focal neurological deficits, or other symptoms suggestive of an intracranial lesion;
- had an intracranial space-occupying lesion detected on computed tomography (CT) or were clinically suspected to have an ICSOL;

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- underwent multiparametric MRI, including conventional MRI, DWI, ADC mapping, and MRS; and
- provided written informed consent to participate in the study.

Exclusion criteria

Patients were excluded if they:

- had contraindications to MRI (e.g., cardiac pacemaker, cochlear implant, ferromagnetic intracranial clips, or other incompatible metallic implants);
- had severe claustrophobia that prevented MRI examination;
- had poor-quality or incomplete MRI examinations unsuitable for analysis;
- had previously undergone surgery, chemotherapy, or radiotherapy for the intracranial lesion before MRI evaluation;

Participant selection

A consecutive sampling technique was used. All eligible patients presenting during the study period who fulfilled the inclusion criteria and provided informed consent were enrolled consecutively until the required sample size of 80 participants was achieved.

Bias

Several measures were implemented to minimize potential sources of bias. Consecutive recruitment of eligible patients reduced selection bias. Standardized MRI acquisition protocols were followed for all participants to reduce measurement bias. Image interpretation was performed using predefined imaging criteria, and histopathological diagnosis served as the reference standard whenever tissue diagnosis was available. Data were recorded using a standardized case record form to ensure consistency and completeness.

Study size

The study included 80 patients**,** representing all eligible patients presenting during the study period who met the inclusion criteria and consented to participate. Because intracranial space-occupying lesions requiring multiparametric MRI are relatively uncommon, a consecutive sampling approach was adopted to maximize recruitment and ensure adequate representation of the spectrum of lesions encountered in routine clinical practice.

Data collection

Demographic information, including age and sex, was obtained from patient records. Clinical data, including presenting symptoms and neurological findings, were collected through clinical examination and medical records. All participants underwent conventional MRI, DWI, ADC mapping, and MRS using the institution's standard neuroimaging protocol.

The following variables were recorded:
Conventional MRI characteristics (lesion location, size, signal intensity, contrast enhancement, and perilesional edema);
Diffusion characteristics using DWI;
Intra-lesional and peri-lesional ADC values ($\times 10^{-3}$ mm²/s);
Spectroscopic metabolites, including choline (Cho), N-acetylaspartate (NAA), creatine (Cr), Cho/NAA ratio, and Cho/Cr ratio;
Final diagnosis based on histopathological examination, wherever available.

Variables

The **primary outcome** was the diagnostic performance of multiparametric MRI in differentiating infective and neoplastic intracranial space-occupying lesions.
The **exposure variables** included conventional MRI findings, diffusion restriction patterns, ADC values, and MRS metabolite concentrations and ratios.
The **predictor variables** included patient age, sex, lesion location, lesion type, tumour grade, ADC values, choline concentration, NAA concentration, creatine concentration, Cho/NAA ratio, and Cho/Cr ratio.
Potential confounding variables included lesion size, perilesional edema, and prior medical history. No effect modifiers were specifically evaluated.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using IBM Statistical Package for the Social Sciences (SPSS) version **25.0** (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD)**,** while categorical variables were summarized as frequencies and percentages. Comparisons between categorical variables were performed using the Chi-square test**.** Continuous variables were compared using the Mann–Whitney U test**,** Wilcoxon signed-rank test, or Kruskal–Wallis test**,** as appropriate. A p-value <0.05 was considered statistically significant.

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Ethical consideration

The study was approved by the Institutional Ethics Committee**.** The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and institutional research guidelines.

Informed consent

Written informed consent was obtained from all participants before enrolment. For patients who were unable to provide consent because of impaired consciousness or neurological deficits, informed consent was obtained from their legally authorized representatives before participation in the study.

Results

During the study period, **94 patients** with suspected intracranial space-occupying lesions were assessed for eligibility. Of these, **10 patients** were excluded because they did not meet the inclusion criteria, including previous treatment for intracranial lesions (n = 4), contraindications to MRI (n = 3), and incomplete MRI examinations (n = 3). An additional **4 patients** declined to participate. Consequently, **80 eligible patients** were enrolled and underwent conventional MRI, diffusion-weighted imaging, apparent diffusion coefficient mapping, and magnetic resonance spectroscopy. All enrolled participants completed the imaging protocol and were included in the final statistical analysis. Histopathological confirmation was available for all participants included in the study.

The study population consisted of 80 patients presenting with clinical features suggestive of ICSOLs. The participants' ages ranged widely, with a calculated mean of 49 ± 16.8 years, and the cohort was perfectly balanced in gender distribution with equal proportions of males (n = 40) and females (n = 40). Based on radiological and histopathological confirmation, the lesions were categorized into Malignant (35%), Benign (28.7%), Infective (25%), and Metastasis (11.3%). Among neoplastic cases, 80% (24/30) were high-grade tumours. Meningioma was the most frequent specific histopathological diagnosis (20%), followed by Glioblastoma Multiforme (17.6%) and Tuberculoma (17.5%). Age distribution varied significantly by etiology, with benign lesions predominating in the 61–70-year bracket and metastatic lesions peaking between 51–60 years. Morphological assessment using conventional sequences revealed significant associations between signal intensity and lesion etiology ($p < 0.05$). Notably, 100% of malignant lesions were hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Conversely, benign lesions demonstrated a strong tendency toward T1 isointensity (91.3%) (Table 1).

Table 1. MRI characteristics of Benign, Malignant, Infective, and Metastatic lesions

MRI Feature		Benign (n=23)	Malignant (n=28)	Infective (n=20)	Metastasis (n=9)	p-value
T1 Signal	Isointense	91.3%	0.0%	-	-	<0.001*
	Hypointense	8.7%	100.0%	-	-	
T2 Signal	Hyperintense	91.3%	100.0%	75.0%	-	0.002*
	Hypointense	8.7%	0.0%	25.0%	-	
DWI Pattern	Restriction Complete Restriction	91.3%	-	-	-	<0.001*
	Patchy Restriction	-	75.0%	-	-	
	Rim Restriction	-	-	70.0%	66.7%	

Post-contrast imaging revealed intense heterogeneous enhancement in 40% of cases, which was typical of high-grade necrosis and neovascularization, while intense homogeneous enhancement strongly correlated with meningiomas. Diffusion restriction patterns correlated significantly with both etiology ($p < 0.001$) and tumour grade ($p = 0.014$). Complete restriction was predominantly observed in benign lesions (91.3%), while high-grade malignancies predominantly exhibited patchy restriction (83.3%), and metastases frequently demonstrated rim restriction (66.7%). Quantitative ADC assessment revealed distinct intra-lesional and peri-lesional differences. The overall mean intra-lesional ADC was $0.8 \pm 0.2 \times 10^{-3}$ mm²/s, while the peri-lesional ADC was significantly higher at $1.5 \pm 0.3 \times 10^{-3}$ mm²/s. Paired Wilcoxon analysis confirmed that peri-lesional ADC was significantly higher than intra-lesional ADC across all subgroups ($p < 0.001$) (Table 2).

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Table 2. ADC assessment of Benign, Malignant, and Infective lesions

Parameters		Benign	Malignant	Infective	p-value
ADC Values (Mean)	Intra-lesional	0.85	0.89	0.70	<0.001
	Peri-lesional	1.65	1.53	1.39	<0.001
MRS Metabolite Ratios (Mean)	Cho / NAA	8.47	3.01	0.82	<0.001
	Cho / Cr	13.11	2.15	1.87	<0.001

This gradient successfully distinguished the cellular tumour core from surrounding vasogenic edema in high-grade tumours (Intra-lesional: 0.87 ± 0.23 vs. Peri-lesional: 1.57 ± 0.14 x 10^{-3} mm^2/s, $p < 0.001$). Spectroscopic profiling demonstrated significant variations in absolute metabolite concentrations and ratios ($p < 0.001$, Kruskal-Wallis test). Metastatic lesions exhibited the highest absolute Choline levels (135,043.78 ± 87,129.09), followed by benign lesions (113,604.83 ± 12,478.27). Paradoxically, malignant lesions demonstrated the lowest mean Choline level (89,599.29 ± 59,327.85). In terms of metabolite ratios, benign lesions exhibited the highest mean values (Cho/NAA: 8.47 ± 2.25; Cho/Cr: 13.11 ± 5.14), driven largely by the near-complete absence of N-acetylaspartate (NAA) in extra-axial meningiomas. Infective lesions demonstrated the lowest ratios (Cho/NAA: 0.82 ± 0.29; Cho/Cr: 1.87 ± 0.66). No statistically significant linear association was found between the specific WHO grade and metabolite ratios within the neoplastic cohort ($p > 0.05$, Mann-Whitney U test).

Discussion

The demographic profile of the study aligns with regional data, though the prevalence of Meningioma (26.3%) was higher than that reported by Gupta et al., who found metastases to be the most common (9). The strong association of T1 hypointensity with malignancy (100% in the study) corroborates the findings of Soorya et al. and reinforces the utility of conventional sequences for preliminary categorisation (10). Diffusion characteristics of the study highlight the critical role of ADC in distinguishing tumour components. The finding that peri-lesional ADC is significantly higher than intra-lesional ADC ($p<0.001$) in high-grade tumours is consistent with Gupta et al. and Lee et al (9,11). This gradient helps distinguish the cellular tumour core (restricted diffusion, low ADC) from peritumoral vasogenic edema (facilitated diffusion, high ADC). In contrast, infiltrative edema often shows lower ADC values, aiding in differentiating Gliomas from Metastases.

A defining finding of this study is the seemingly paradoxical behavior of Choline in high-grade malignancies. The standard radiological literature suggests that malignant tumours exhibit elevated Choline Levels due to rapid membrane turnover (12). However, in the cohort, malignant lesions demonstrated the lowest mean absolute Choline levels. This is attributable to the specific composition of the malignant group, which was dominated by high-grade glioblastomas characterized by extensive central necrosis. When MRS voxels capture necrotic tissue, the metabolic signal universally drops out, including Choline (12). Conversely, the benign cohort—dominated by solid, highly cellular meningiomas devoid of necrosis—produced consistently strong Choline signals. Because these extra-axial tumours lack background neuronal tissue (and thus lack NAA), their Cho/NAA ratios (8.47 ± 2.25) were mathematically elevated compared to intra-axial malignant gliomas (3.01 ± 1.10) (13,14). Compared with the literature, our study's findings regarding Cho/Cr ratios align with those of Ahmed et al., who distinguished neoplastic from non-neoplastic lesions based on elevated ratios (13). However, unlike Arevalo-Saenz et al., who correlated specific ratio cut-offs with glioma grade, our study did not find a linear correlation between ratios and WHO grade, suggesting that tumour heterogeneity (necrosis vs. solid components) significantly influences spectral readouts (14).

The finding in this cohort study was that malignant tumours showed lower absolute Choline levels than benign lesions, a result that initially seems counterintuitive, given that Choline is a marker of cellular turnover. However, this is likely explained by the specific composition of our tumour groups. The malignant group consisted largely of high-grade glioblastomas, characterised by extensive central necrosis. When spectroscopic voxels include these necrotic areas, the metabolic signal 'drops out,' artificially lowering the average Choline readings. In contrast, our benign group was dominated by meningiomas. These are solid, highly cellular tumours that typically lack necrosis. As a result, they produced consistently strong Choline signals due to their dense cell membrane turnover, resulting in higher absolute values than those of the heterogeneous, necrotic malignant tumours.

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Generalizability

The findings of this study apply to adult patients with intracranial space-occupying lesions evaluated at tertiary care teaching hospitals equipped with multiparametric magnetic resonance imaging facilities and histopathological diagnostic services. The results support the use of conventional magnetic resonance imaging combined with diffusion-weighted imaging, apparent diffusion coefficient mapping, and magnetic resonance spectroscopy for the preoperative characterization of intracranial lesions. However, the findings should be generalized with caution to primary or secondary healthcare settings, pediatric populations, or institutions without access to advanced neuroimaging techniques.

Conclusion

The characterization of ICSOLs is significantly improved by a multiparametric MRI approach. While conventional MRI provides anatomical localisation, DWI and quantitative ADC mapping effectively differentiate cellular cores from edema. MRS offers unique metabolic insights; however, results must be interpreted with caution. Specifically, low Choline levels in high-grade tumours should raise suspicion of necrosis rather than benignity. The integration of these modalities is essential for accurate preoperative diagnosis and grading.

Limitations

This study has several limitations. First, it was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Second, the heterogeneous distribution of lesion types resulted in relatively few cases within some diagnostic categories, potentially affecting subgroup analyses. Third, absolute metabolite concentrations obtained by magnetic resonance spectroscopy may have been influenced by voxel placement, partial-volume effects, and intralesional necrosis. Finally, long-term clinical outcomes and post-treatment follow-up were not evaluated, limiting assessment of the prognostic value of multiparametric magnetic resonance imaging.

Recommendation

Multiparametric magnetic resonance imaging should be incorporated into the routine preoperative evaluation of patients with suspected intracranial space-occupying lesions whenever advanced imaging facilities are available. The combined assessment of conventional magnetic resonance imaging, diffusion-weighted imaging, apparent diffusion coefficient mapping, and magnetic resonance spectroscopy can improve diagnostic accuracy and facilitate appropriate treatment planning. Future multicenter prospective studies with larger sample sizes are recommended to validate these findings and establish standardized imaging protocols for differentiating infective and neoplastic intracranial lesions.

List of abbreviations

ADC – Apparent Diffusion Coefficient
Cho – Choline
Cr – Creatine
CT – Computed Tomography
DWI – Diffusion-Weighted Imaging
ICSOL – Intracranial Space-Occupying Lesion
MRI – Magnetic Resonance Imaging
MRS – Magnetic Resonance Spectroscopy
NAA – N-Acetyl Aspartate
SPSS – Statistical Package for the Social Sciences

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Data availability statement

The datasets generated and analysed during the current study are not publicly available due to institutional restrictions and the presence of sensitive patients' information, but are available from the corresponding author on reasonable request and with permission from the Institutional Ethics Committee.

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Competing interests

The authors have declared that no competing interests exist.

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Original Article

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