

Original Research

## A Study of Brain Metastases and Tuberculomas Examination Using MRS and DWI

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### ABSTRACT

**Objective:** The present comparative study evaluates brain tuberculomas and metastasis using a combined analysis of MRS and DWI in the Pakistan context.

**Materials & Methods:** The present comparative study was conducted at the Department of Neurology, Aziz Fatimah Medical and Dental College Faisalabad, Pakistan. This comparative prospective analysis also included 118 newly diagnosed, untreated individuals who were suspected or confirmed to have nervous system tuberculosis (NST) using sophisticated MRI methods such as DWI and MRS. Linear regression was utilized to compare tuberculomas based on the apparent diffusion coefficient value of high-grade gliomas and metastatic lesions.

**Results:** Tuberculomas displayed predominantly isointense (61%) and hypointense (58.3%) signals on T1W and T2W images, respectively. Metastases showed a higher occurrence of T2 hyperintensity (61.6%) and T1 hypointensity (46.2%). Neurocysticercosis consistently appeared hypointense and hyperintense across all imaging modalities. High-grade gliomas were primarily hypointense on T1W (60%) & hyperintense on T2W (100%) images. Abscesses were uniformly hyperintense on T2W images. Mean ADC values were highest in neurocysticercosis ( $1.64 \times 10^{-3} \text{ mm}^2/\text{s}$ ) and lowest in abscesses ( $0.396 \times 10^{-3} \text{ mm}^2/\text{s}$ ). MRS revealed distinctive metabolite ratios, with high NAA/Cr & NAA/Ch0 in neurocysticercosis and elevated Ch0/Cr in high-grade gliomas.

**Conclusion:** There is no discernible benefit to using DWI to distinguish tuberculomas from gliomas and metastases. It is possible to distinguish tuberculomas from gliomas and metastases using their distinct metabolite pattern on MRS.

**Keywords:** Brain Tuberculomas, Metastasis, Combined Analysis, MRS (Magnetic Resonance Spectroscopy), DWI (Diffusion Weight Imaging).

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## INTRODUCTION

Brain metastases and tuberculomas represent two very important health issues worldwide, as well as in Pakistan.<sup>1</sup> Accurate diagnosis and differential diagnosis of these conditions are important for treatment planning. A couple of modern neuroimaging modalities, such as Diffusion-Weighted Imaging and Magnetic Resonance Spectroscopy, are useful in this regard in differentiating these lesions.

Metastatic lesions from other primary sites of cancer in the body; such as melanoma, lung cancer, and breast cancer are among the most frequent sites. Clinically, it can present with headaches, seizures, cognitive disturbances, or focal neurological deficits. Granulomatous lesions due to infection by *Mycobacterium tuberculosis*. Common among people of high-prevalence regions for tuberculosis such as those seen in Pakistan. Symptoms can be similar to brain metastases, making clinical differentiation challenging.<sup>3-4</sup>

Provides metabolic information about brain lesions by measuring the concentration of specific metabolites. N-acetyl aspartate (NAA), choline (Cho), creatine (Cr), lactate, and lipids are common metabolites that are evaluated. Increased Cho and decreased NAA are common in brain metastases, but tuberculomas frequently display a lipid-lactate peak as a result of caseation necrosis. Measures the diffusion of water molecules within tissue, providing information about cellularity and the integrity of cell membranes. Brain metastases usually exhibit high cellularity, leading to restricted diffusion and hyperintense signals on DWI.<sup>5</sup>

In developing countries, tuberculosis (TB) of the central nervous system (CNS) is a major source of illness and mortality.<sup>6</sup> In developed nations, TB is also on the rise, particularly when underlying human immunodeficiency virus infection is present. About 1% of all TB infections are CNS infections, which are characterized by neurological impairments and need prompt diagnosis and

treatment to prevent long-term harm. Conglomerated lesions of fibroblasts, Langhans giant cells, and lymphocytes around central caseation necrosis are common features of intracranial tuberculomas.<sup>7</sup>

Tuberculoma often manifests as a nodular or isolated lesion; multilocular or en plaque variants are less prevalent. Tuberculoma may be present extra-axially in fissures and cisterns, as well as elsewhere in the brain parenchyma. Although rare in affluent nations, tuberculomas account for 30% of all cerebral mass lesions there.<sup>8</sup> The global comeback of CNS TB is a result of the HIV epidemic. The chemical makeup of the brain is revealed by proton MRS, which can be quite useful in the tuberculoma diagnosing process. By estimating the apparent diffusion coefficient, DWI gives quantitative information on the tiny mobility of water molecules in a tissue (ADC).<sup>9</sup>

Differentiating intracranial tuberculoma from other space-occupying brain lesions is necessary to expeditiously start antituberculous therapy for this potentially curable condition. Diagnosing brain tuberculomas without meningitis is challenging since several differential diagnoses may be made using conventional imaging techniques like CT and MRI.<sup>5</sup> In many situations, MRI cannot reliably identify tuberculomas since there is known to be significant overlap with other focal brain lesions. The necessity for biopsy, an intrusive process with dangers, would be avoided with a non-invasive tuberculoma diagnosis. Furthermore, perfusion MRI, MR spectroscopy (MRS), susceptibility-weighted imaging (SWI), diffusion-weighted imaging (DWI), and MR spectroscopy (DWS) are imaging modalities that may help improve the identification of these brain lesions.<sup>10</sup>

## MATERIALS & METHODS

### Study Setting, Duration, and Sample

The study was conducted after receiving ethical approval from the institutional ethics council at Aziz Fatimah Medical and Dental College Faisalabad, Pakistan. Patients consent from the Neurology department, (n=118) patients, (n=90) males and (n=90) females, ranging in age from one year to seventy-six (45 years old on average), were prospectively assessed with MRS and DWI from January 2024 to June 2024. In every instance, the patient's attendant gave their informed permission.

### Inclusion Criteria

The study includes the following patients: Patients with CNS tuberculosis confirmed cases or probable cases. A CT scan may reveal lesions other than metastases, such as rings or disc-enhancing lesions (i.e., people with no known cancer elsewhere in the body).

### Exclusion Criteria

Patients with metallic implants, pacemakers, and other conditions in which MRI is not recommended as a whole were not included in the research.

### Data Collection

For each examination, the present study used a superconducting magnetic resonance imager (T1.5) equipped with a standard head coil. Detailed imaging protocols and parameters were established to ensure consistency and accuracy in data acquisition across all patients.<sup>11</sup> By adhering to this standardized protocol, the present study ensured the reliability and reproducibility of the data collected, providing a robust foundation for distinguishing various brain pathologies through advanced imaging techniques. Moreover, using a picture archiving and communication system (PACS) workstation, areas of interest (ROI) were

placed on the lesion to create apparent diffusion coefficient (ADC) maps and determine ADC values. ADC was measured from the solid components in lesions with both cystic and solid parts.

Further, water signal suppression was used in a point-resolved spectroscopic sequence for multivoxel three-dimensional chemical shift imaging. Acquisition of spectroscopic data was done after the administration of 0.1 mmol/kg gadodiamide. (Omniscan; GE Healthcare). For patients with primary brain tumors diagnosed via MRI, surgery or stereotactic biopsy was performed, particularly in lesions involving critical brain areas. For metastasis diagnosis, a thorough assessment was conducted to locate the primary tumor. If the primary site remained unidentified, stereotactic biopsy was performed, with histology confirming metastatic lesions. The data collected from the MRI, DWI, and MRS scans were subjected to comprehensive analysis to differentiate between the various brain pathologies.

### Data Analysis

Data analysis was done using imaging and spectroscopic data in the form of quantitative measurement and statistical analysis in GraphPad Prism 10. The morphological features and metabolite data were summarized using tables. For the metabolite ratios – NAA/Cr, NAA/Cho, Cho/Cr, and the ADC values vs. other metabolite ratios, the relationships were evaluated using Pearson correlation coefficients. This was a multifaceted approach to data analysis that provided an in-depth view of imaging and spectroscopic features that can contribute much toward the diagnosis of the type of brain lesions and contribute strongly to the differentiation between various pathologies.

## RESULTS

### Clinical and Demographic Features of Patients (N=118) Age Distribution

The participants in this study ranged in age from 2 to 78 years (mean age of 46). Patients with tuberculosis were between 2 and 78 years old (average age of 42). For these 82 patients, the definitive diagnosis was established through clinical and radiological follow-up, with a mean follow-up duration of 12 months (range: 5–20 months).

### Gender Distribution

The study group consisted of 72 males (61%) and 46 females (39%) resulting in a male-to-female ratio of 2.2:1.

### Clinical Futures

Besides routine MRI, 118 patients with ring/disc-enhancing lesions on CT scan or who have known or suspected CNS TB underwent evaluation with advanced MRI methods, including DWI, MRS, and SWI. Of 118 patients, 74 had tuberculomas at the time of final diagnosis, and 26 had metastatic disease. Twelve were diagnosed as gliomas, six as neurocysticercosis (NCC), and two as pyogenic abscesses. The fifth number was achieved on histopathological examination and confirmed the final diagnosis in patients with tuberculomas ( $n = 5$ ), 18 with metastases, 12 with gliomas, and three with pyogenic abscesses (total = 38; 32% incidence). Additionally, the final diagnosis was verified by radiological response to antitubercular therapy (ATT) in 75 patients with tuberculomas and to albendazole in 7 patients with neurocysticercosis (NCC) ( $n = 82$ , or 69%).

### Focal Brain Lesions

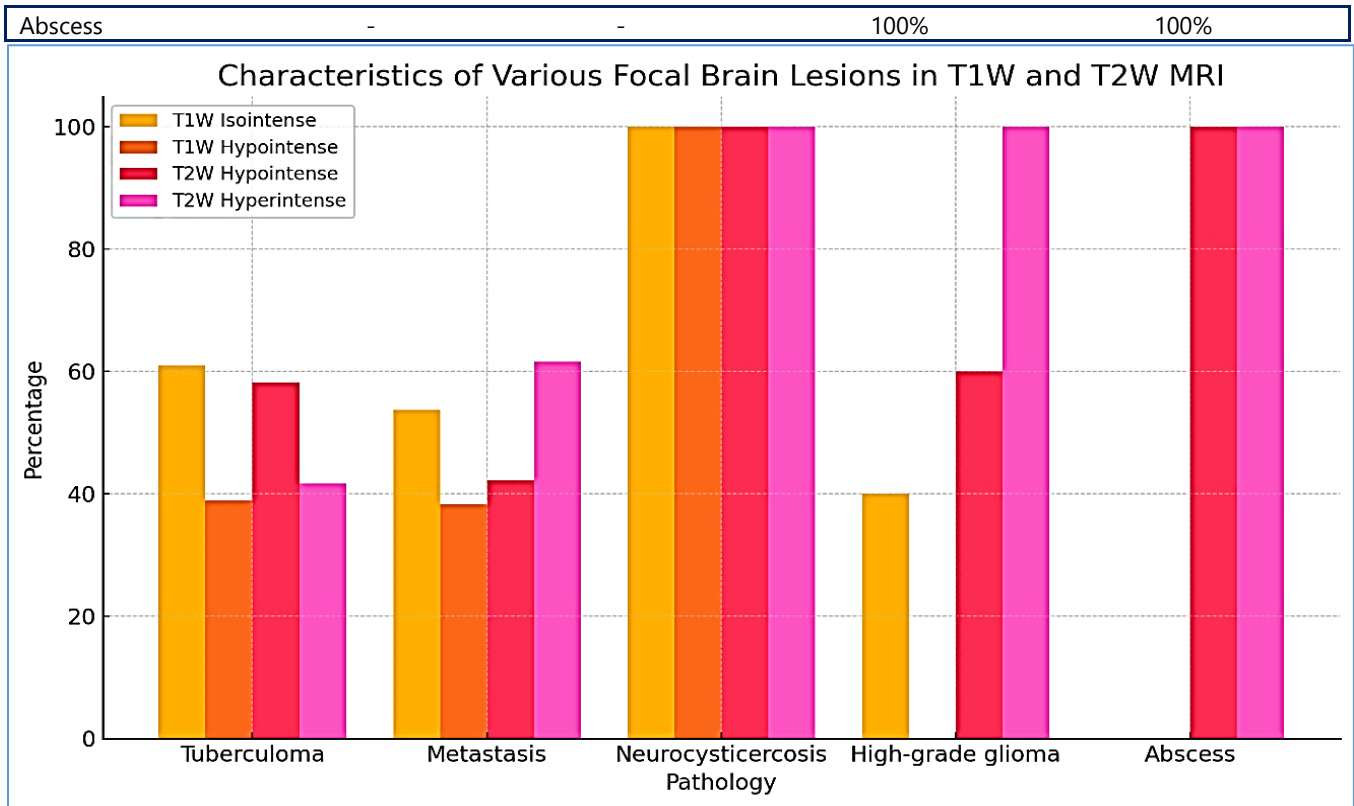
Table 1: Features of different focal brain lesions in

T1-weighted (T1W) and T2-weighted (T2W) magnetic resonance imaging sequences.

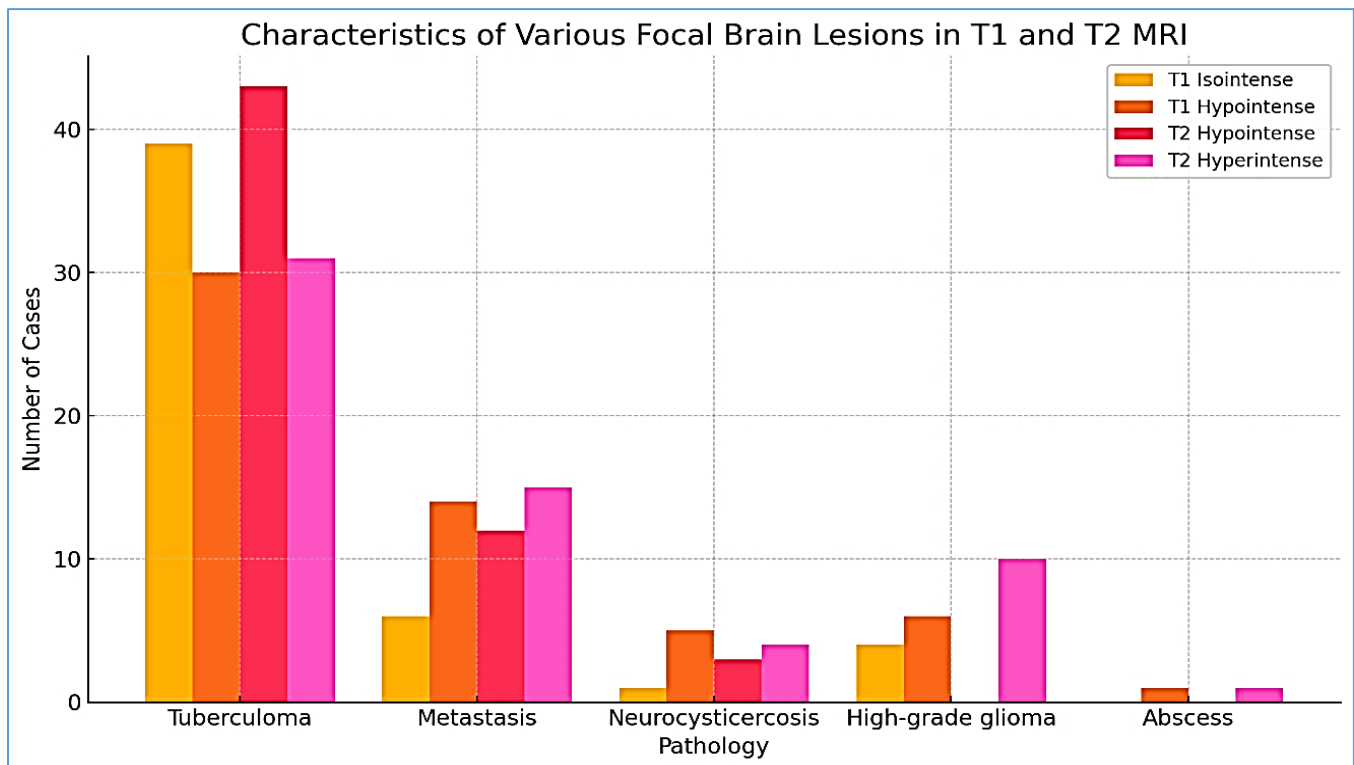
Figure 1 highlights the contrast enhancement pattern known as “ring enhancement” which was most commonly observed in all types of brain lesions. T2W hypointense tuberculomas exhibited considerably greater ADC values than T2W hyperintense tuberculomas, with tuberculomas having an ADC value of  $1.027 \times 10^{-3} \text{ mm}^2/\text{s}$ . The bar chart and the data interpretation highlight the importance of using both T1W and T2W MRI sequences to identify and differentiate various brain lesions. While some lesions, such as metastases and high-grade gliomas, show a higher tendency for hyperintensity on T2W images, others, like tuberculomas, exhibit more varied signal intensities. The consistency in the imaging characteristics of neurocysticercosis and abscesses emphasizes the need for comprehensive imaging protocols to accurately diagnose and treat these conditions.

Figure 2 shows the number of cases that are isointense or hypointense on T1-weighted images and hypointense or hyperintense on T2-weighted images for each pathology. T1 Tuberculomas and high-grade gliomas show significant hypointensity. Metastases and neurocysticercosis have mixed appearances. Tuberculomas and metastases exhibit a preference for hyperintensity. High-grade gliomas and abscesses are consistently hyperintense. Demonstrates varied intensities across all imaging types, reflecting different lesion stages or types. The honestly uncomplicated chart and its analysis underscore that both T1 and T2 MRI sequences are needed when a valid diagnosis of contrasting multiple brain lesions is realized.

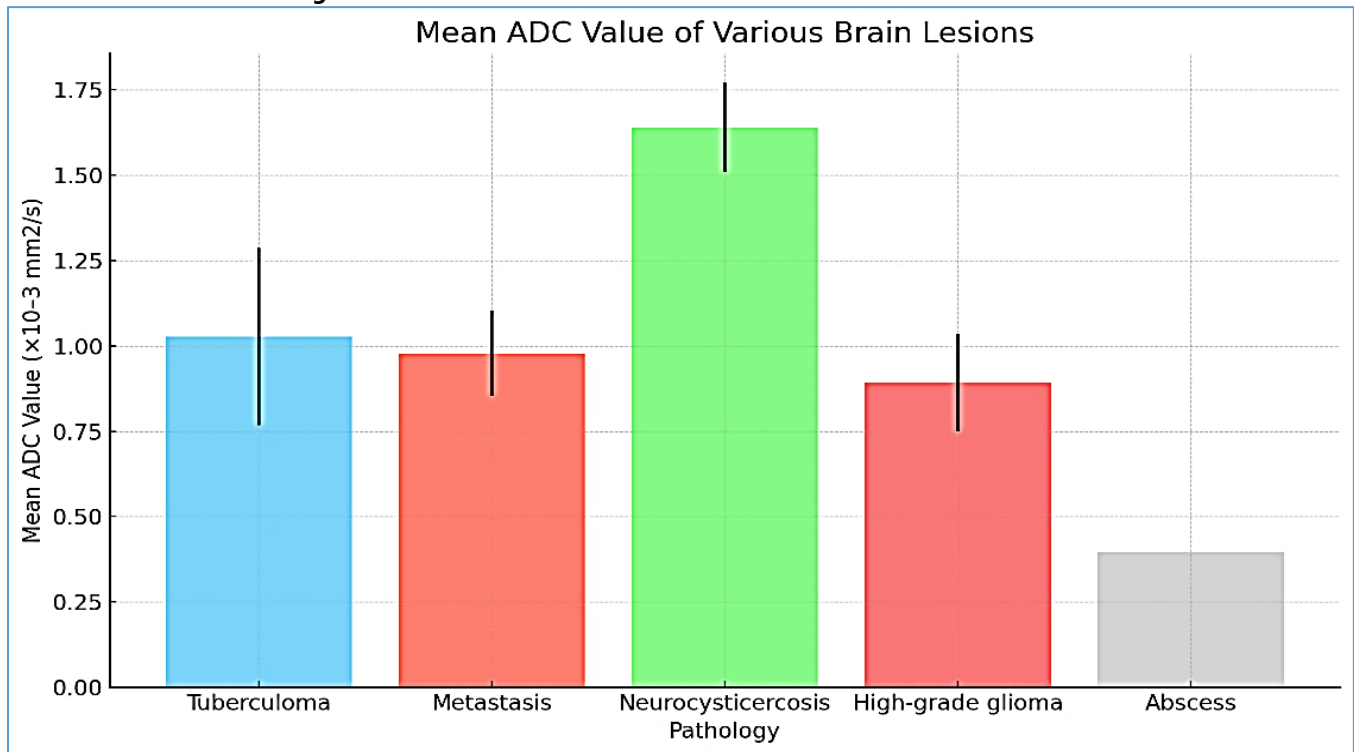
Pathology	T1W Isointense	T1W Hypointense	T2W Hypointense	T2W Hyperintense
Tuberculoma	61%	39%	58.3%	41.7%
Metastasis	53.8%	38.4%	42.2%	61.6%
Neurocysticercosis	100%	100%	100%	100%
High-grade glioma	40%	-	60.0%	100%



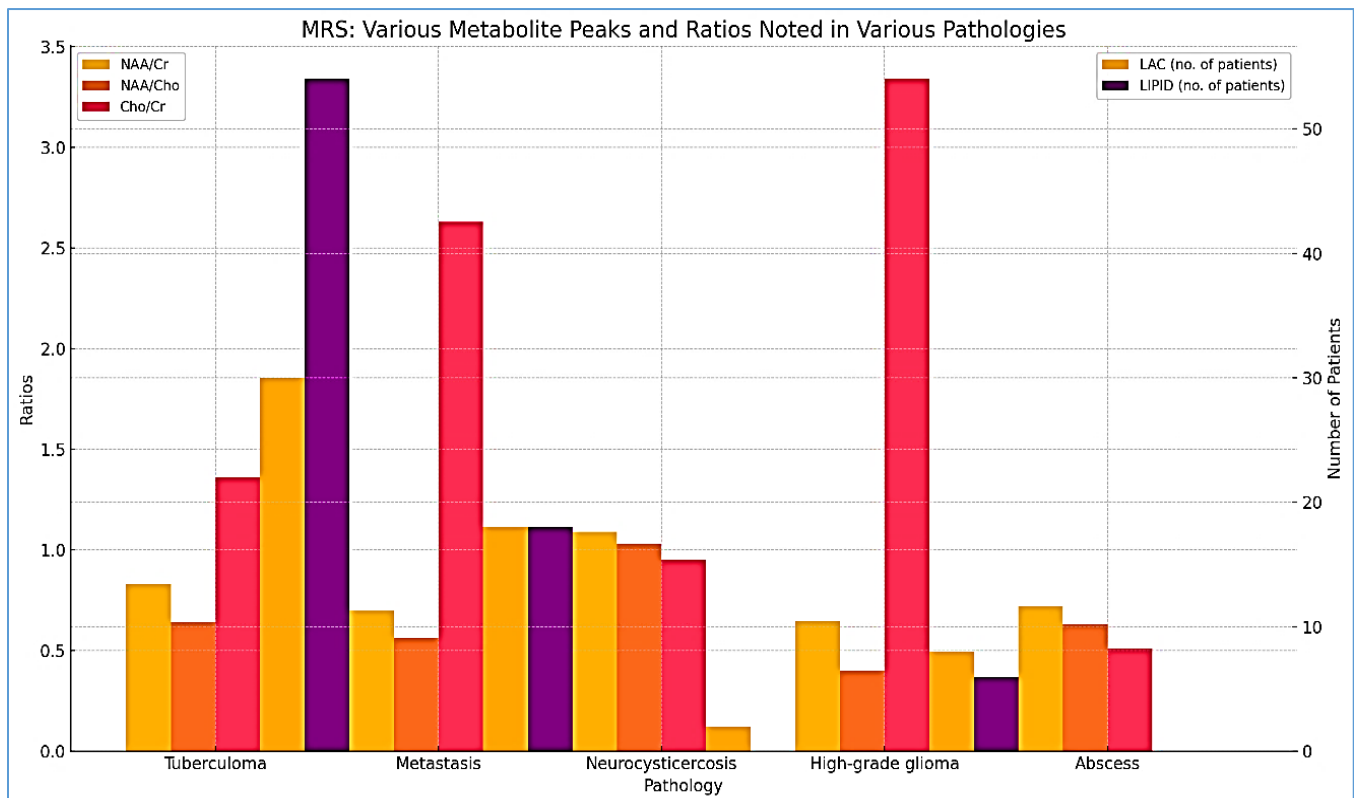
**Figure 1:** Characteristics of Various Focal Brain Lesions in T1W and T2W MRI.  
 Note: T1W: T1 weighted; T2W: T2 weighted.



**Figure 2:** Characteristics of Various Focal Brain Lesions in T1 and T2 MRI.



**Figure 3:** Mean ADC Value of Various Brain Lesions.



**Figure 4:** MRS: Various Metabolite Peaks and Ratios Noted in Various Pathologies.

## ADC Values of Various Types of Brain Lesions

Figure 3 was plotted denoting the average ADC values of various types of brain lesions; it also exposes their standard deviations. The chart depicted the average ADC values (in  $\times 10^{-3} \text{ mm}^2/\text{s}$ ) for various pathologies, distinguishing among them based on their apparent characterization and diffusion in MRI.

## DISCUSSION

The current study comparatively assesses brain lesion differentiation through advanced imaging: *in vitro* proton Magnetic Resonance Spectroscopy ((MRS) and *in vivo* Diffusion-Weighted Imaging (DWI). In the following sections, the principal results will be discussed in the light of literature about metabolic and diffusion characteristics that identify each pathology. The mean ADC value for these lesions is  $1.027 \times 10^{-3} \text{ mm}^2/\text{s}$  with a standard deviation of 0.26. This is consistent with findings by Saurya et al. (2024), which highlight the variability in ADC values of tuberculomas due to differences in cellularity and the presence of necrosis.<sup>13</sup> The mean ADC value is  $0.978 \times 10^{-3} \text{ mm}^2/\text{s}$  (SD 0.124838). Lower ADC values in metastases are often attributed to higher cellularity compared to primary brain tumors, as described by Sobeh.<sup>14</sup> The mean ADC value is significantly higher at  $1.64 \times 10^{-3} \text{ mm}^2/\text{s}$ , with a standard deviation of 0.13. This agrees with Gupta et al, who reported high ADC values for cysticercosis lesions, which only underscores their cystic nature with low cellularity. The mean ADC value comes to about  $0.892 \times 10^{-3} \text{ mm}^2/\text{s}$  with a standard deviation of 0.143. Lower ADC values suggest higher cellularity and increased mitotic activity, which studies confirm. The mean ADC value lies lowest at  $0.396 \times 10^{-3} \text{ mm}^2/\text{s}$ , which was predicted considering the high cellular content and viscosity of abscesses that would restrict diffusion. This was supported by research by Dahlberg.<sup>15</sup> Another study aimed to assess the

potential of radiomics features extracted from various MRI sequences, including T1W, T2W, T2W FLAIR, T1W post-contrast, and ADC maps, to differentiate between tuberculomas, high-grade gliomas, and brain metastases.<sup>15</sup> The current study's findings are consistent with earlier research showing that tuberculomas are common in poor nations and can exhibit fluctuating MRI signals, which can cause an overlap in the imaging phenotype between gliomas and metastases. For early anti-tubercular medication, reduced patient morbidity and mortality, and to avoid needless neurosurgical excision, an accurate MRI diagnosis is essential. There were 185 participants in the retrospective research. Photos underwent preprocessing techniques such as resampling, co-registration, z-score normalization, and skull-stripping. Lesion segmentation was done automatically, and then radiomics feature extraction, train-test split, and feature reduction were carried out. A range of machine learning methods were taught and evaluated using features from both single and multiple modalities. Using SHAP values, the best-performing model's explainability was determined.<sup>15</sup> With an AUC of 0.96, accuracy of 0.923, and Brier score of 0.23, the Extra Tree classifier trained on ADC map characteristics proved to be the most effective in differentiating tuberculomas from high-grade gliomas and metastases. With remarkable accuracy and AUC ratings, the study showed that radiomics characteristics may successfully distinguish between tuberculomas, metastases, and high-grade gliomas. The most reliable predictors of the target variable were features that were taken from ADC maps. This work emphasizes the utility of radiomics in the differential diagnosis of frequent intraparenchymal mass lesions seen in clinical practice, such as high-grade gliomas, metastases, and tuberculomas. Utilizing radiomics characteristics, especially those from ADC maps, can help determine the best course of action for care and contribute to an accurate MRI diagnosis.<sup>15</sup>

## CONCLUSION

This study highlights the utility of conventional MRI characteristics combined with ADC values and MRS metabolite profiles in differentiating among various brain lesions. Mostly isointense on T1W images, but hypointense on T2W images; mean ADC values indicated moderate cellularity. Frequently hypointense on T1W images and hyperintense on T2W images; the ADC values overall were lower, reflecting higher cellularity. All the imaging modalities depict signals that are relatively consistently hypointense and hyperintense with high ADC values, probably because of lesser cellularity; markedly hypointense on T1W and hyperintense in T2W images with low ADC values and increased Cho/Cr ratios, which is probably indicative of high cellularity and hence malignancy; uniformly hyperintense in T2W images with the lowest ADC values, indicating high cellularity and restricted diffusion. MRS metabolite analysis further differentiates these lesions, showing unique patterns of NAA, Cho, and Cr. Such imaging modality integration provides additional accuracy to diagnosis and clinical management. Therefore, studies in larger populations with more advanced techniques are highly recommended shortly to validate such observations for diagnostic guidelines.

## List of Abbreviations

DWI: Diffusion-weighted imaging  
 CNS: Central Nervous System  
 MRS: Magnetic Resonance Spectroscopy  
 NST: Nervous System Tuberculosis  
 MRI: Magnetic resonance imaging  
 NAA: N-acetyl aspartate  
 TB: Tuberculosis  
 PACS: Picture Archiving and Communication System.

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## Additional Information

### Disclosures:

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**Data Availability Statement:** The data that support the findings of this study are available from the corresponding author, Dr. Atif Maqsood, upon reasonable request. Due to the sensitive nature of the patient data and privacy agreements, access to the data was granted under the condition that the requester agrees to maintain confidentiality and use the data solely for academic and research purposes. Data was shared in a de-identified format to protect the privacy of the study participants.

**Conflict of Interest:** The authors declare that there is no conflict of interest regarding the publication of this study. All research was conducted independently, and there were no financial or personal relationships that could have influenced the outcomes of this research. Any potential conflicts were managed following the ethical standards of the institutions involved.

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Financial Relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other Relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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### **AUTHORS CONTRIBUTION**

<b>Sr.#</b>	<b>Author's Full Name</b>	<b>Contribution to Paper in Terms of:</b>
1.	Atif Maqsood & Faizan Aslam	Study design, Data Collection, and methodology.
2.	Muhammad Absar Alam & Nadia Zulfiqar	Data Analysis & Graphics.
3.	Mubarak Ali Anjum	Introduction and References.
4.	Muhammad Asif Javed	Paper writing, Grammar.