



# The Evaluation of Integrated Perfusion - Weighted Imaging Diffusion and Magnetic Resonance Spectroscopy Methods Accuracy for Brain Neoplasms Diagnosis Compared to Pathology Findings

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## Abstract

**Background:** MRI has a vital role in the assessment of brain neoplasm. Conventional MRI has limited specificity. The combination of MRI using diffusion-weighted imaging, perfusion-weighted imaging and magnetic resonance spectroscopy allows more accurate assessment of the tissue microenvironment. **Objective:** The role of diffusion-weighted Perfusion - Weighted Imaging, and Magnetic Resonance Spectroscopy techniques to evaluate the Accuracy of Brain Neoplasms Diagnosis. **Method:** This project is based on cross-sectional design. The population of this study were 80 patients with brain tumors that have been indicated for MRI test in the period of sampling which was during February 2023 to July 2023. The data-collecting technique was done by the researcher using a questionnaire, observation, and laboratory findings. The questionnaire was designed and copied by the researcher. MRI examinations was performed using MRI 1.5 T scanner (Philips MULTIVA systems) using a phase array 6 channels head coil at the radiology department. The data had encoded and then entered into the statistical program (SSPS version 26). **Results:** A total 80 of six equally collected group samples were investigated radiographically for brain (8, 9, 17, 31, 7, and 8 patients) respectively after the inclusion and exclusion criteria. The age of each study sample was normally distributed and ranged from 10 to 86 years without significant differences between them (P-value= 0.16). One patient out of 80 was diagnosed incorrectly when using MRS sequence. Therefore, the achieved total accuracy, sensitivity and specificity are 97.61%, 100% and 87.5% respectively. The achieved p-value among study's groups is 0.6. Although it is highly significant and accurate in the MRS procedure, additionally, the p-value when implementing the three independent sample ANOVA-test between the Choline, creatine and NAA is high significant with p value choline being 0.0001 and p-value for NAA being 0.0024 which means that there are highly significant differences between tissue brain groups. 80 patients were diagnosed correctly when using combining diffusion, perfusion and MRS sequence. Therefore, the achieved total accuracy, sensitivity and specificity are 100%, 100% and 98.9% respectively. Additionally, the achieved p-value of overall diagnosing result is 0.75 which confirms that no patients failed to diagnose by combining DWI, PWI and MRS than separate protocol. **Conclusion:** In this study we found that it is possible to diagnose brain malignancies with a greater level of sensitivity and accuracy by combining perfusion, diffusion-weighted imaging (DWI), and magnetic resonance spectroscopy (MRS). It has been found that using the CBF and CBV parameters for diagnosing brain lesions is more effective than using the MTT and TTP parameters. The NAA and Choline parameters are superior to the Creatinine parameter in terms of their ability to accurately diagnose brain lesions. The combination of DWI, MRS, and MRP predicted 100% sensitivity and Specificity 98.6% and accuracy 100% for the differentiation of the type of brain tumor. These cutting-edge MRI techniques eliminated the need for invasive treatments like transcranial biopsies.

**Keywords:** MRI, Perfusion sequence, Diffusion sequence, DWI, Brain tumor, Glioma, GBM, meningioma, Astrocytoma, NAA, Choline, Creatinine, MTT, TTP, CBF, CBV.

## 1. Introduction

Brain tumors are serious life-threatening disease and risky illnesses. The most destructive disease is uncontrolled, the Cancerous brain tumors are uncontrolled, leading to a very short life expectancy. In their highest grade, cancerous brain tumors are overwhelming (Petrosyan et al., 2022). Brain neoplasms are one of the leading causes of cancer-related morbidity and mortality (Romano et al., 2023). Brain tumors account for a large fraction of years (Datta, Sears, Cortopassi, Woolard, & Angelastro, 2021), The incidence of neoplasms, which is 24 per 100,000 person-years, is higher than that of neoplasms from other sites, which increases the possibility of potential life loss and lowers patients' quality of life. (Allison's, 2021). A brain tumor is a group of irregular cells in the brain that forms a mass, any expansion in such an area will cause serious problems (Roetzer-Pejrimovsky et al., 2022). The diagnosis and classification of a brain tumor should be based on the World Health Organization (WHO) 2021 classification system (Louis et al., 2021). In the United States, about 23,000 patients were diagnosed with a brain tumor in 2015 (Wen et al., 2020). According to cancer data from 2017, Brain tumors are one of the leading causes of cancer-related indisposition, morbidity, and death in both children and adults worldwide (Wen et al., 2020). WHO defines 150 brain tumor types, assigning grades I to IV based on malignancy and potential progression. An integrated approach is mandatory for 19 types. (Allison's, 2021). (Irene Grazzini, 2023). The annual incidence of primary and secondary central nervous system neoplasms ranges from 10 to 17 per 100,000 persons (Wen et al., 2020). WHO report shows tumors are the top cause of death before 70 in 112 states and 23 others. (Granata et al., 2023; Rumgay et al., 2022; Sung et al., 2021). Brain tumor classification is among the most crucial aspects of the medical field (Ait Amou, Xia, Kamhi, & Mouhafid, 2022). Brain tumors burden health and public healthcare, with 308,102 new cases and 251,329 deaths in 2020 due to poor prognosis. (Tong, McCullagh, & Iv, 2020). MRI improves with diagnosis, therapy planning, and treatment evaluation (Volterrani et al., 2020). Brain vital organ, contains nerve cells, tissues and unique capacities; abnormal cell growth causes tumors, leading to cancer (Ahmad, Sun, You, Palade, & Mao, 2022). The BBB is necessary for the central nervous system to maintain a stable microenvironment (Jafari, Pourseif, Barar, Rafi, & Omid, 2019). Tumors damage BBB integrity, causing heterogeneous vasculature with non-uniform permeability and active efflux. (Arvanitis, Ferraro, & Jain, 2020). MRI images detect tumor growth and progress in brain tumors, aiding diagnosis, grading, treatment, and response assessment in intracranial lesions. (Alshammari et al., 2021; Sawlani et al., 2020). Misdiagnosis of brain tumors leads to incorrect medical intervention, reducing patient survival chances; accurate diagnosis is crucial for proper treatment planning. (Hussain et al., 2022). MR imaging studies brain tumors' anatomy, physiology, metabolic activity, and hemodynamics, making it the primary diagnostic modality for brain tumors. (Scola et al., 2023). MRI technology advances improve accuracy, but specificity remains a challenge. (Du, He, & Lin, 2022). MR imaging widely used for evaluating intracranial tumors. (Khan et al., 2022). Conventional MR imaging provides a highly detailed anatomic depiction of the human body and structural details of lesions in the neuraxis; however, its specificity is limited (Barkovich & Barkovich, 2019; Traboulsee & Li, 2008). MRI improves tumor detection and post-therapy monitoring, but biopsy remains the gold standard. (X. Li et al., 2023). Advanced MR techniques enable noninvasive evaluation of brain microstructures, cellularity, physiology, perfusion, and metabolism, aiding differential diagnosis and monitoring treatment

effects and disease progression. (Auer, 2021). Advanced imaging techniques like MRS, MRP, DWI, and DTI aid in diagnosing brain lesions, especially in patients without malignancy. (Dickerson & Srinivasan, 2017). In our study, Advanced techniques and protocols in magnetic resonance imaging enhance accurate diagnosis and treatment planning in clinical neuro-oncology practice. Combining DWI, PWI, and MRS protocols aids in brain tumor examination, to evaluate the Accuracy of Brain Neoplasms Diagnosis. The Main Objective of our study is to evaluate the Accuracy of diffusion-weighted Perfusion - Weighted Imaging, and Magnetic Resonance Spectroscopy techniques for Brain Neoplasms Diagnosis.

## 2. Research Methods

### Material and methods

A total of 80 patients with positive sign of brain neoplasma who had been referred to the radiology center at Baghdad Health Directorate (AL-Alamy Hospital for Specialized Surgeries) IRAQ. The research was studied at the period of February 2023 to July 2023 and followed all ethical requirements. For all patients a combined imaging protocol comprising under routine conventional MRI (T1, T2, FLAIR), DWI, PWI and MRS was done before surgery at the radiology department using a 1.5 T scanner (Philips MULTIVA systems) with standard multiple (6) channel head coils all patient underwent in a single session.

All lesion were confirmed histologically and grouped according to the type of neoplasma (type of malignancies) the tumour in 8 patients as astrocytoma, ependymoma 9 patients, 17 GBM, 31 glioma, 7 meningioma and 8 metastasis according to the classification of the WHO. MRI imaging.

### Patient exam position

MRI examinations conducted on a 1.5-Tesla MRI system in the supine position Conventional T1, T2, and fluid-attenuated inversion recovery images obtained. After a complete description of the study to the patients, informed consent was obtained from all the enrolled patients. During the whole MRI examination, all patients were instructed to breathe normally and not move. A hospital gown or loose-fitting clothing was worn by the enrolled patients. the head of the patient was examined first, the body of the patients were encased in the tube and were expected to be completely kept still for a time period of 40 minute while the machine created images of the head. Brain MRIs were done on the exam room sofa, with the patient in supine, the arms were on the sides of the trunk, the head placed within the head coil and the ears plugged to reduce the noise as the machine-made thumping, knocking, and humming sound. The head balanced in such a way that the interpapillary line was paralleled to the couch the patient's head fixed in the head vacuum cushion and the motion artifacts avoided. In the longitudinal alignment, a red laser light appears is different from the horizontal alignment light.

### Conventional MRI sequences

Conventional MRIs protocol T1 weighted image comprised slice thickness 5mm slice gap 0.0 TR4000 Parameter short TE 25 flip angle 90, matrix size 320x320 for T2WI long TE of 200 msec long TR 7000msec flip angle 130 degree were used then T2 FLAIR, the scan parameter repetition time TR 9000 and echo time TE 130, matrix size 320x320, FOV210-230 and T1WI SE (slice thickness 5mm slice gap 0.0- 1mm, matrix size 320x320 acquired before and after contrast agent administration. all slices orientation axial plane are insufficient in clarity of anatomical region of mass, therefore axial TWI ax post-contrast Gadolinium contrast agent 0.1-0.2 mmol/kg body weight was done through intravenously manually injection.

**DWI- MRI Diffusion weighted image**

For DWI-ADC mapping, axial plane echo-planar imaging (EPI) sequence with b of 0 s/ mm<sup>2</sup> as the reference image factor=500,1000 s/mm<sup>2</sup> was applied and ADC mapping was performed with field of view (FOV) 24 cm, slice thickness 5mm 192 x 192 matrix, TR 7000, TE 110 and NEX 1; all diffusion gradients were performed from x-y-z planes. Acquired image were transferred to work station. ADC measurement was performed by manual implantation of region of interest (ROI) to the solid parts of mass lesions with restricted diffusion and lower ADC values were considered to be malignant.

**Perfusion weighted image MRP**

For MRP, DSC is acquired with rapid echo planar imaging (EPI) and relies on a drop in T<sub>2</sub>\* signal after passage of a gadolinium-based contrast bolus, 0.1-0.2 mmol/kg with manual injection was used as the contrast agent Gadolinium (Gd.) contrast Gadovist (1mL). Using a standard dose 0.1 mmol/kg - 0.2mmol/kg body. Dynamic scanning for acquiring a series of MRIs for 40 dynamic scan, every nine milliseconds and eight-tenths he took an image with one slice for each phase, Axial plane EPI sequence was applied, post-processing of all images were acquired in the Philips work-station. ROI's size 2.5x2.5x5.0 mm were used intra lesion. CBV, CBF, the mean transit time of contrast agent (MTT) and time to peak (TTP) were expressed automatically by the system. Four ROI's as an average were used for perfusion analysis of each mass lesions. A normal contralateral reference ROI was also applied for statistical correlation. Lesions with lower MTT and TTP, highly vascular with elevated CBV were diagnosed as malignant.

**MR Spectroscopy methods MRS**

MRS was performed by using point-resolved spectroscopy (PRESS) with a volume of interest (VOI), 20 x 20 x 20 cm standard voxel sizes for the single voxel spectroscopy and presaturation bands placed around the VOI. Depending upon the tumor and the lesion size, we have positioned the possible voxel within the solid tumoral or lesional area avoiding areas of cysts, normal appearing brain parenchyma, and scalp or skull base contamination. Automatic shimming of the linear x, y, and z channels was used to optimize field homogeneity, water resonance and water suppression pulses were optimized for the consistent water saturation. Proton spectrum was recorded in axial plane with repetition time (TR), 2000 ms; echo time (TE), 288 ms; FOV, 224 x 224 mm; 5 mm slice thickness slice gap 0.0; matrix size 90 x 92. The duration of scan for both TE acquisitions was about five minutes. N-Acetyl aspartate (NAA) at 2 ppm, creatine (Cr) at 3-3.1 ppm, choline (Cho) at 3.2 ppm, were analyzed. NAA/Cr, Cho/Cr ratio quantifications were also performed. Contralateral reference voxel was placed just symmetric to the center of the original brain lesion for the statistical comparison. High Cho metabolites, depressed NAA peak, high

intraregional NAA/Cr and Cho/Cr ratio, and depressed NAA/Cr were considered as malignant. All protocols and methods performed for each patient at the same time probably (40 minutes). Medical diagnoses for tumors with and without using the new model are taken and get a comparison with gold standard histopathological grading to get sensitivity and specificity.

**Data collection**

The data-collecting technique was collected by the researcher using a questionnaire, observation, and laboratory findings. The questionnaire was designed and copied by the researcher and it contains two parts: the demographic part of the patient, for example, the age were considered from 12 years old and above and gender, and the observation part of the patients, such as Size of mass, Site of mass, BMI, weight and height, smoking, drinking alcohol Clinical presentation: nausea, vomiting, speech problems, vision problems, headache After the proposal was approved, an official letter was received from the educational vice of the faculty of allied Medical Sciences of Tehran University of Medical Science, and then permission to gather samples was obtained from Baghdad Health Directorate (AL-Alamy Hospital for Specialized Surgeries). With a proposal and authorization from the university. The images of MRI were collected and evaluated. Data entry was done by SPSS version 26 and analyzed by the same software.

**Data analysis**

Data were analyzed and reported only for patients who complete the trial statistical analysis of data, and performed use in order to evaluate the level of agreement of sensitivity, specificity, Positive and negative predictive value and overall accuracy are necessary for all methods in evaluating brain tumors. After collecting the data, Descriptive statistics like Mean, percentage difference, and significant tests were evaluated. The mean and standard deviations of the average. An unpaired two-tailed Student's t-test were used. The data had encoded and then entered into the statistical program (SSPS version 26).

**3. Result**

**Baseline demographic characteristics of study's sample**

A total 80 of six equally collected group samples were investigated radiographically for brain (8, 9, 17, 31, 7, and 8 patients) respectively after the inclusion and exclusion criteria. The age of each study samples was normally distributed and ranged from 10 to 86 years without significant difference Table1 shown age: Mean values of the males and females in the study's samples (n=80). Between them (P-value= 0.16) which reflecting the matching purpose of samples collection, as shown in Table 1. Figure 1, shows the distribution of male/female among the study's groups.

**Table 1: Baseline demographic characteristics of the study's samples (n=80)**

Study groups of the collected dataset (Age and Gender)												
Histopathology	Astrocytoma		Ependymoma		GBM		Glioma		Meningioma		Metastasis	
Male(M)/ Female(F)	M (4)	F (4)	M (5)	F (4)	M (10)	F (7)	M (18)	F (13)	M (4)	F (3)	M (4)	F (4)
Mean ± SD	28.67±19.64	29.57±19.64	30.38±7.93	29.50±8.23	56.60±12.93	55.63±13.61	41.38±17.24	42.34±18.68	45.00±14.56	58.00±11.17	52.00±26.74	49.50±27.03
Range (Min-Max)	51 (10-61)		22 (17-39)		43 (26-69)		67 (14-81)		37 (30-67)		69 (17-86)	
P-value	0.16											

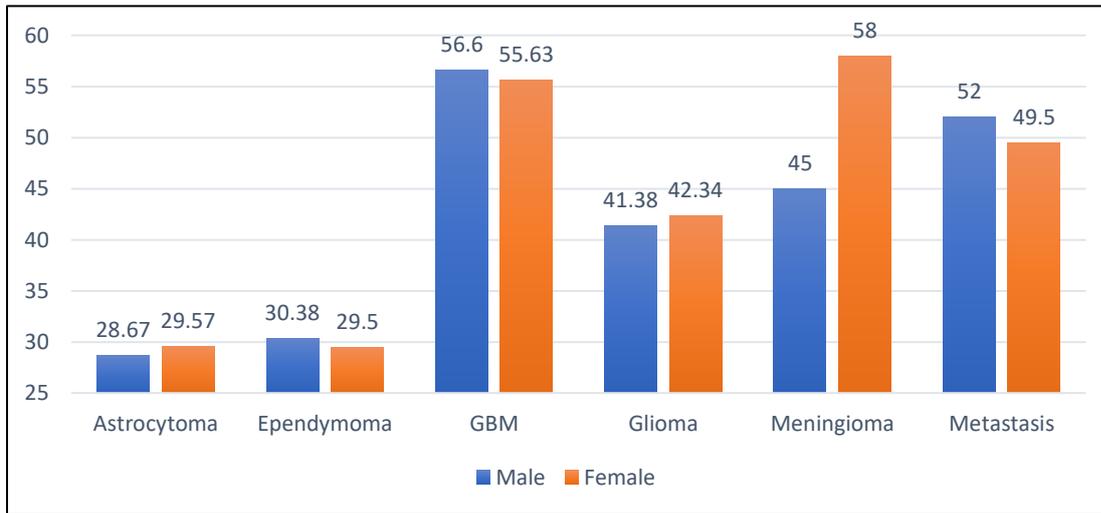


Figure 1: Mean values of the males and females in the study's samples (n=80).

### Statistical Analysis in Methods

The collected data was entered, double checked and analysed using IBM SPSS Software version 26. Descriptive statistics that were qualitatively summarized the characteristics of the collected data were used in this study. Additionally, ANOVA test, Independent Samples t-Test, Paired sample t-test were used to determine the significance among study's groups. Furthermore, the utilized p-value that indicates the differences among study's groups, was suggested to be less than 0.05 in this study. In our study conventional MRI the assessment diagnosis brain tumors are limited sensitivity, specificity and accuracy 62.5%, 58.3% and 60% respectively to diagnosis brain neoplasms finding.

Table 2: ANOVA test among histopathology of the brain groups when using conventional MRI sequences of the study's sample.

Area	0.701
Cut off	0.1415
Total	60%
Sensitivity	62.5%
Specificity	58.3%
P-Value	0.21

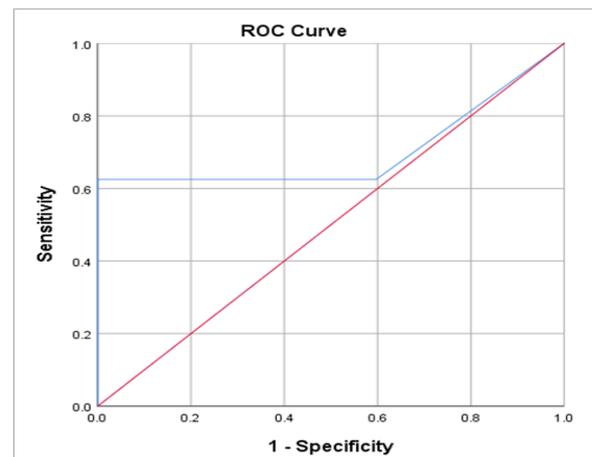


Figure 2: Receiver Operating Characteristic Curve analysis (ROC) of Diagnosing by using conventional MRI sequences.

Most of the impediments that have limited the use of perfusion MRI can be overcome to allow integration of these methods into modern neuroimaging protocols such as MR Spectroscopy sequence. Furthermore, Implementation ANOVA test shows that the NAA and Choline parameters are more efficient in diagnosing brain lesions than Creatine parameter, as reveals in Figure 3. Figure 4 shows the ROC curve of diagnosing the study's samples by M

Table 3: ANOVA test among histopathology of the brain groups when using MRS sequence of the study's sample (n=80).

Study groups of the collected dataset													
Histopathology (n=80)	Astrocytoma (n=8)		Ependymoma (n=9)		GBM (n=17)		Glioma (n=31)		Meningioma (n=7)		Metastasis (n=8)		P-Value
NAA ppm	0.009±0.01 2		0.012±0.00 7		0.004±0.00 38		0.005±0.0 03		0.0032±0.0 007		0.01±0.01 4		0.024(S)
Creatine ppm	0.0026±0.0 035		0.018±0.02		0.0038±0.0 025		0.014±0.0 3		0.004±0.00 32		0.004±0.0 09		0.29
Choline ppm	0.01±0.01		0.028±0.01 6		0.012±0.00 9		0.004±0.0 04		0.004±0.00 5		0.005±0.0 05		0.0001(HS)
	TP/FP											Total Accuracy	
	8	0	9	0	17	0	31	0	6	1	8	0	
Accuracy	100%		100%		100%		100%		85.71%		100%		97.61%
Area	0.986												
Cut off	0.956												
Sensitivity	100%												
Specificity	87.5%												
P-Value	0.6												

Brain metabolites (NAA, Creatine, Choline) ppm

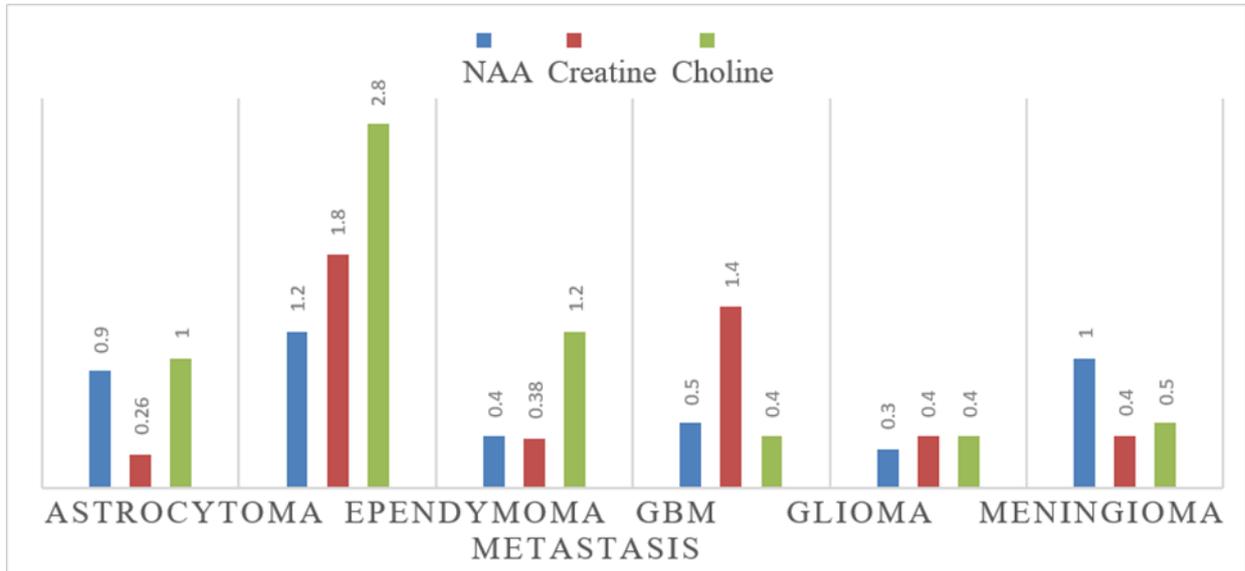


Figure 3: Normalized mean values of histopathology of the brain groups by using MRS scan.

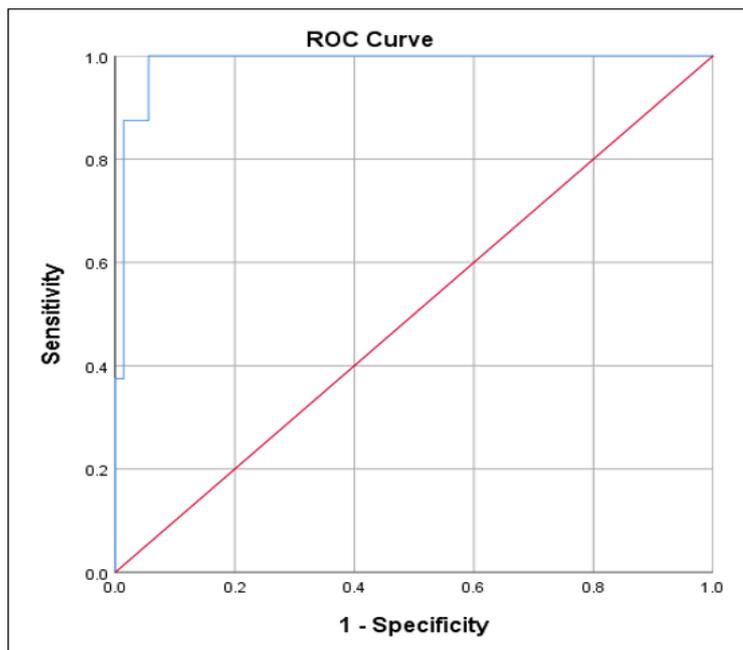


Figure 4: Receiver Operating Characteristic Curve analysis (ROC) of Diagnosing by MRS Sequence.

The combination of magnetic resonance spectroscopy and perfusion with DWI can increase sensitivity and positive predictive value to diagnose the brain tumours, as demonstrated in Table 4. Where, all patients are diagnosed correctly with the achieved total accuracy, sensitivity and specificity are 100%, 100%, and 98.6% respectively. Additionally, the achieved p-value of overall diagnosing result by

perfusion is 0.75, and this confirms that It Is possible to differentiate brain tumours in such cases that are difficult to diagnose by conventional magnetic resonance imaging. Figure 5 shows the ROC curve of diagnosing the study's samples by combining DWI, perfusion and MRS sequences.

Table 4: ANOVA test among histopathology of the brain groups when combining Diffusion, Perfusion and MRS sequences of the study's sample.

Area	1
Cut off	0.1415
Total Accuracy	100%
Sensitivity	100%
Specificity	98.6%
P-Value	0.75

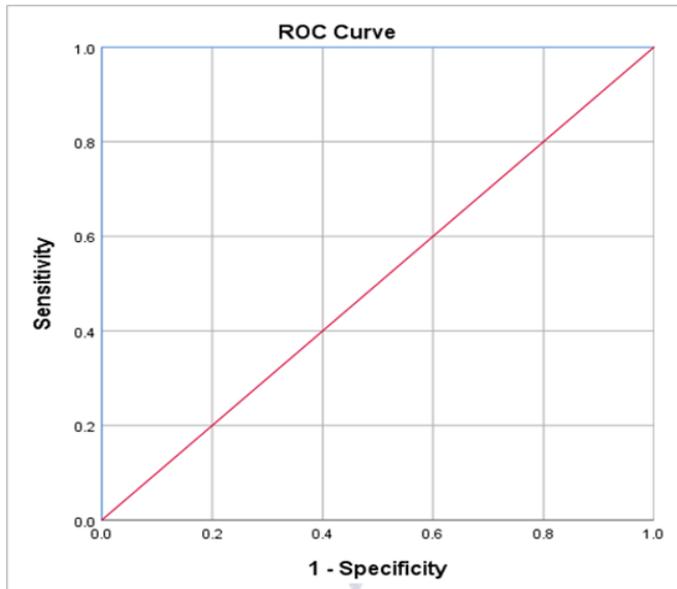
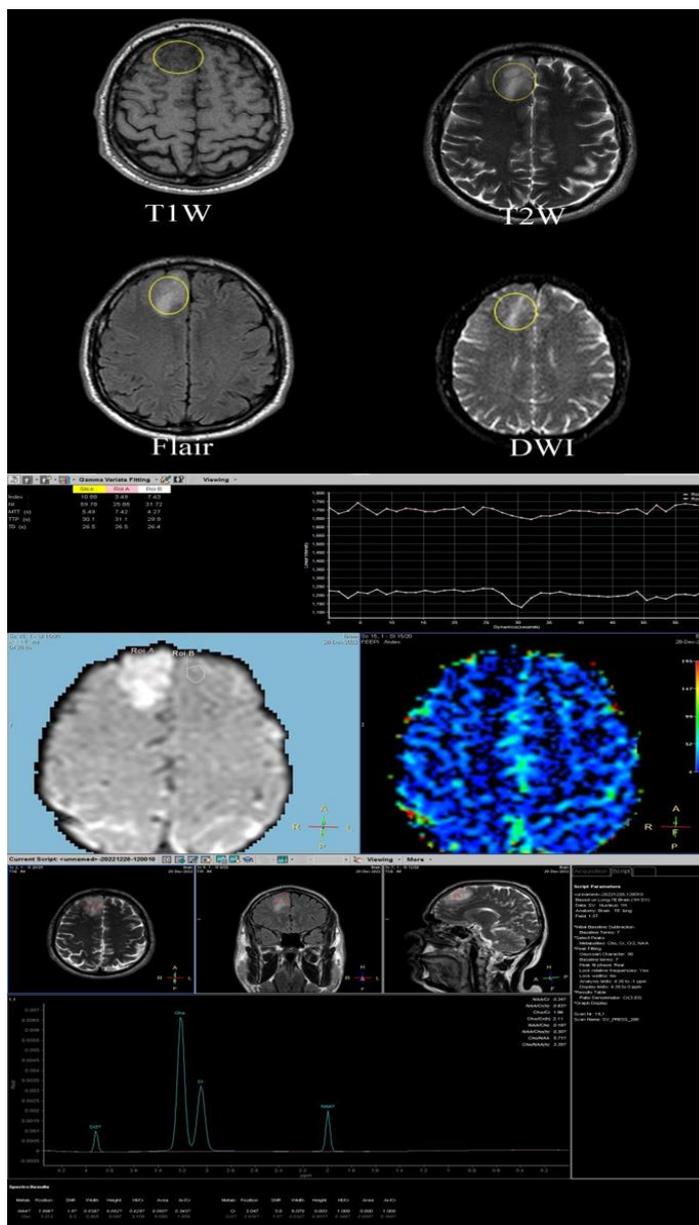
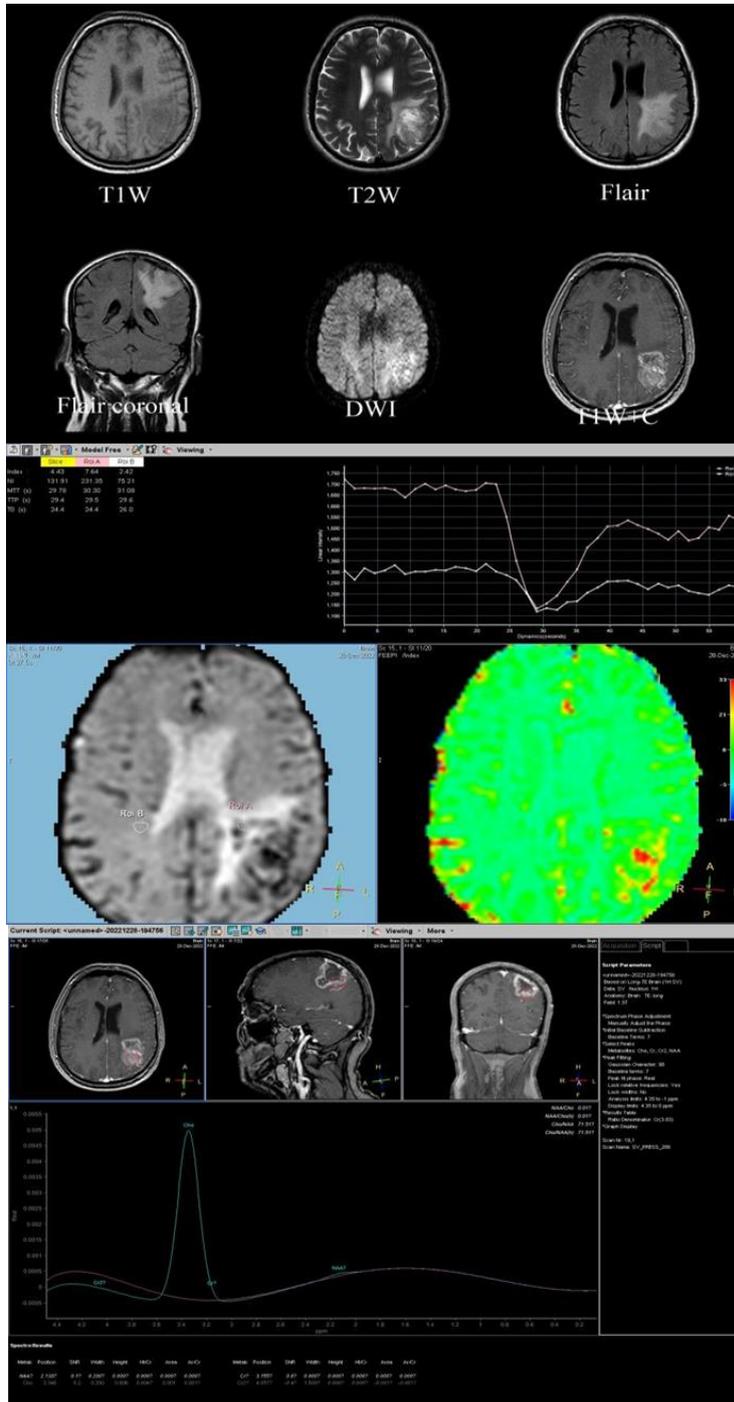


Figure 5: Receiver Operating Characteristic Curve analysis (ROC) of Diagnosing by combining DWI, PWI Perfusion and MRS.

### Case Presentation



Case 1: Male, Glioma, 40 Yrs. MRI sequence T1, T2 flair DW post contrast and spectroscopy show: Rt. frontal lobe mass show hypo-intense on T1, hyper-intense on T2 and flair show restricted DW with increased CBF, CBV in PWI and increased in choline and creatinine.



Case 2: Male, GBM, 62 Yrs. MRI Sequences T1, T2, FLAIR, DWI, post contrast, perfusion and MR spectroscopy LT parietal lobe mass show hypo intense in T1W hyper intense in T2W and flair restricted diffusion enhancement post contras. In PWI increase CBF, CBV MRS Show increased choline and decreases NAA.



correctly with the achieved total accuracy, sensitivity and specificity are 100%, 100%, and 98.6% respectively. Additionally, the achieved p-value of overall diagnosing result by perfusion is 0.75, and this confirms that It Is possible to differentiate brain tumors in such cases that are difficult to diagnose by conventional magnetic resonance imaging. Which is similar to the study of (Aydın, Aydın, Birgi, & Hekimoğlu, 2019), found out that in differentiating neoplastic-non-neoplastic brain lesions the combination of DWI, MRS and MRP was more beneficial than using them alone. MRS yielded 77% sensitivity and 63% specificity; while the combination of DWI and MRP predicted 100% sensitivity and 88% specificity. By the combination of either DWI or MRS, MRP and MRS or DWI+MRS+MRP revealed 100% sensitivity and 100% specificity.

The most common histological tumor type observed in our study were the tumors of neuroepithelial origin, which included 31(38.75%) patients of gliomas, then followed by 17(21.25%) patients of glioblastoma multiforme. and 9 patient (11.25%) with Ependymoma, 8 (10%) patients of astrocytoma, and 8 patients (10%) with Metastasis as well. The other histologic tumor type was tumors of meningeal tumors such as meningioma which accounted for 7 (8.75 %) patients. Similar findings were noted in studies done by Ng S et al (Ng et al., 2020) and Zouaoui S et al. (Zouaoui et al., 2012).

## 5. Conclusion

Advanced MRI techniques are required in many clinical cases where conventional MRI fails to differentiate malignant lesions such as glioblastomas and metastases. 1H-MRS, DWI, DTI and DSCE MRI has been incorporated in the clinical routine to improve specificity and provide an insight into the underlying biological characteristics of brain tumors. In this study we found that it is possible to diagnose brain malignancies with a greater level of sensitivity and accuracy by combining perfusion, diffusion-weighted imaging (DWI), and magnetic resonance spectroscopy (MRS) more accurate diagnosis. It has been found that using the Index and NI parameters for diagnosing brain lesions is more effective than using the MTT and TTP parameters. The NAA and Choline parameters are superior to the Creatinine parameter in terms of their ability to accurately diagnose brain lesions. The combination of DWI, MRS, and MRP predicted 100% sensitivity and Specificity 98.6% and accuracy 100% for the differentiation of the type of brain tumor. These cutting-edge MRI techniques eliminated the need for invasive treatments like transcranial biopsies.

## List of abbreviations

Choline (Cho)  
Diffusion-Weighted Imaging (DWI)  
Echo-Planar Imaging (EPI)  
Gadolinium (Gd.)  
N-Acetyl Aspartate (NAA)  
Point-Resolved Spectroscopy (PRESS)  
Receiver Operating Characteristic Curve Analysis (ROC)  
Region of Interest (ROI)  
Repetition Time (TR)  
Time to Peak (TTP)  
Volume of Interest (VOI),

## Ethical consideration

The Common Ethics Committee of Tehran University of Medical Sciences (IR. TUMS. SPH. REC. 1401. 295), and the Research and Ethics Committee of Baghdad Health Directorate, Center of

Training and Researches, Baghdad, Iraq, all were sought for ethical approval to conduct the research. All official agreements were also obtained in this manner

## Compliance with ethical guidelines

All the participants filled the consent form Funding Present research article was extracted from the MSc. thesis of Ms. Azhar Kareem Hasan Al husseini which was compiled to full-fill degree requirements at Tehran University of Medical Science.

## Competing interests

No

## Funding

No

## Author's contributions

All authors contributed to the design and implementation of the research, to the Analysis of the results and to the writing of the manuscript Acknowledgments The authors would like to appreciate all individuals who took part in this research. The Authors would like to appreciate the assistance of the faculty and the staff of Tehran University of Medical Sciences, the School of Allied Medical science, and department of Radiology technology. This study was supported by Tehran University of Medical Sciences

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