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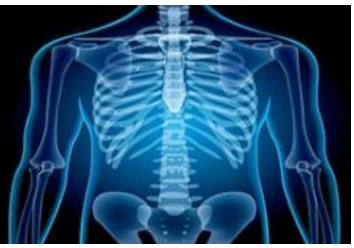

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MR diffusion kurtosis and intravoxel incoherent motion related perfusion imagings in assessment and grading of brain tumors

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Abstract
Background: Primary brain tumors refer to a diversified group of benign as well as malignant neoplasms that arise from the parenchymal tissue of the brain or the nearby components. Neoplasms are a crucial cause of morbidity & mortality in adults as well as children, usually result in marked disabilities and causing high burden in the patient's family along with the health care system. This work aimed to determine the importance of MR Diffusion kurtosis and Intravoxel incoherent motion related perfusion imaging in assessment and grading of brain tumors.
Methods: This prospective study was carried out on 50 cases with histopathologically proven, clinically and or MRI manifested with brain tumors and with no comorbidities. Routine MRI, diffusion kurtosis, PWI and IVIM were performed to all patients.
Results: Regarding assessment of the brain tumors, the estimated conventional diffusion weighted image (DWI) values with 95.22% sensitivity, 80.67% specificity, 96.5% PPV and 40% NPV, the estimated conventional apparent diffusion coefficient (ADC) values with 87.8% sensitivity, 59.56% specificity, 90% PPV and 50% NPV, conventional T_1 with contrast enhancement pattern of the brain tumors with 94.24% sensitivity, 70.44% specificity, 90.1% PPV and 50% NPV, the estimated relative cerebral blood volume (RCBV) values with 96.24% sensitivity, 92.89% specificity, 97.4% PPV and 66.7% NPV, the estimated diffusion kurtosis imaging (DKI) with 97.30% sensitivity, 94.1% specificity, 90.23% PPV and 50% NPV, the estimated advanced diffusion weighted image (IVIM parameter) values with 98.22% sensitivity, 99.23% specificity, 97.5% PPV and 50% NPV, the estimated advanced apparent diffusion coefficient (IVIM parameter) values with 97.83% sensitivity, 91.24% specificity, 90% PPV and 50% NPV, the estimated Diffusion coefficient (D*) (IVIM parameter) values with 89.17% sensitivity, 55.56% specificity, 91.1% PPV and 55% NPV, the estimated perfusion fraction (F%) (IVIM parameter) values with 99.12% sensitivity, 100% specificity, 98% PPV and 79.8% NPV.
The estimated DWI values couldn't predict high grade tumors in our study (P=0.357and AUC=0.650) at cut-off > 0.83 with 90.24% sensitivity, 66.67% specificity, 92.5% PPV and 60% NPV. ADC couldn't predict high grade tumors (P=0.836 and AUC=0.535). (D*) couldn't predict high grade tumors (P=0.752 and AUC=0.556). (F%) predicted high grade brain tumors at cut-off >7.3 with 95.12% sensitivity,100% specificity,100% PPV and 81.8% NPV.
RCBV significantly predicted high grade tumors at cut-off >6.2 with 90.24% sensitivity, 88.89% specificity, 97.4% PPV and 66.7% NPV. DKI significantly predicted high grade tumors at cut-off >286 with 90.24% sensitivity, 44.44% specificity, 88.1% PPV and 50% NPV.
Conclusions: DKI at cut-off >286, Perfusion fraction at cutoff >7.3, RCBV at cutoff > 6.2 and diffusion enhancement can significantly predict high grades of BTs ($p< 0.05$). However, DWI, ADC, and diffusion coefficient D* can't predict high grade of BTs ($p< 0.05$).

Keywords: Diffusion kurtosis, intravoxel incoherent motion, perfusion imaging, brain tumors

Introduction
Primary brain tumors refer to a diversified group of benign as well as malignant neoplasms that arise from the parenchymal tissue of the brain or the nearby components. Neoplasms are a crucial cause of morbidity & mortality in adults as well as children, usually result in marked disabilities and causing high burden in the patient's family along with the health care system [1, 2].
Conventional diffusion weighted imaging (DWI) of 3 orthogonal aspects as well as diffusion

tensor imaging (DTI) aren't completely precise in assessment of the glioma grade or Ki-67 expression. A nuclear Ag that's expressed on any proliferating cell can denote cellular proliferation. The insufficient assessment is due to the fact that the standard DWI & DTI depend on assuming that H_2O diffusion has a Gaussian distribution. Nevertheless, because of the complexity of the structures in the brain tissues and neurons that include the cell membrane, organelles inside the cells, and water element, the diffusion of H_2O molecules deviates from the Gaussian distribution. Thus, reducing the efficiency of traditional DWI and DTI [3-5].

Diffusion kurtosis imaging (DKI) is one of the advanced non-Gaussian diffusion techniques that is suggested to be responsible for such deficiency. It gives a more precise model of diffusion to quantify the deviation from the Gaussian distribution, that's called kurtosis. Through obtaining data for >2 non-zero diffusion gradient factors (b value) in >15 non-linear directions, the kurtosis metrics (that included mean kurtosis (MK), axial kurtosis (Ka) and radial kurtosis (Kr)) and traditional diffusion metrics (that include mean diffusivity (MD), axial diffusivity (Da), radial diffusivity (Dr) and fractional anisotropy (FA)) can be obtained at the same time. Ka is in parallel with the principal direction of diffusion, Kr is upright to the principal direction of diffusion, and MK is the average kurtosis of all directions. So, DKI might be useful in comparison with DWI and DTI for the determination of microstructural alterations in various tissue and cell types [3].

Gliomas refers to a diversified group of tumors having high microstructural complexity and diversity, in particular for higher grade types or gliomas with high cell proliferation rates, that could impede proton diffusion, resulting in higher non-Gaussian and high kurtosis [6].

Intravoxel incoherent motion (IVIM) depends on the use of various b-value DWI or quantitative analysis of H_2O molecules diffusion and microcirculation perfusion of 2 types of moving elements, and providing an easy and accurate evidence for precise diagnosis [7, 8].

This work aimed to determine the role of MR Diffusion kurtosis and IVIM related perfusion imaging in assessment & grading of brain tumors.

The patients and Methods

This prospective study was carried out on 50 of the patients, all ages, both gender, with histopathological proven, clinically and or magnetic resonance imaging (MRI) manifested with brain tumors and with no comorbidities such as decompensated CVS or respiratory disorders, uncontrolled DM, acute kidney failure or acute infectious disease. The study was carried out following approval from the Ethical Committee Tanta University Hospitals. The study was done from February 2021 till May 2023. An informed written consent was taken from the patients or their relatives of the patients.

Exclusion criteria were non cooperative patient who can't still lie during the MRI examination and contraindications to do MRI (Cardiac pacemaker, metallic implants, claustrophobia, MR-incompatible prosthetic heart valves, implanted electric and electronic devices, any kind of ear implants, metallic FB in the eye, insulin pump or drug infusion devices).

All cases underwent full history taking and MRI.

MRI was done using a multi-element phased-array coil was used. Each scan takes a few minutes. MRI was carried out using 3-Tesla MRI scanner. (Magnetom Skyra®, Siemens Healthcare).

Routine MRI

It included these sequences: Axial T_1 fluid-attenuated inversion recovery (T_1-FLAIR), Axial T_2 fast spin echo (T_2-FSE) and Axial T_2 fluid-attenuated inversion recovery (T_2-FLAIR).Injection of Gadolinium-based contrast substance was done The gadolinium-chelate contrast substance; gadopentetate dimeglumine (0.1-0.2 mmol/kg) was administered IV.

Diffusion kurtosis

DKI utilized a SE-EPI diffusion sequence for imaging. Processing of the Diffusion kurtosis data was carried out via diffusion kurtosis estimator, and processing of diffusion weighted images was done.

Perfusion weighted imaging (PWI)

Perfusion assessment was carried out using DSC approach using fast echoplanar T_2-weighted gradient echo sequence. Ten seconds after the beginning of the image acquiring, 1.0 mol/l gadobutrol formula (Gadovist) was divided into two equal volumes and injected simultaneously in antecubital veins and followed by a saline bolus injection (20 ml). Following PWI an after-contrast 3D T_1-weighted sequence was carried out via the use of contrast bolus given before the perfusion examination.

Intravoxel Incoherent motion (IVIM)

Cases were subjected to imaging on a 3T MR system employing head coil adequate for parallel imaging. IVIM imaging was performed using a Stejskal–Tanner diffusion-weighted single-shot SE-EPI pulse sequence. IVIM images were processed using dedicated post processing software for IVIM processing using bi-exponential analyses of DWI sequences, detecting the focus area (ROI). in parts with a high fraction of perfusion on IVIM map, cystic as well as necrotic regions in addition to subarachnoid space were avoided as they cause artifacts in the assessed values. Moreover, we aligned them with T_1-weighted imaging and spatial smoothing was done using a 3 mm full-width-at-50% maximum Gaussian kernel. Cross-modality registration had been done and metric maps were calculated.

Statistical analysis

Data were fed to the computer and analysis was carried out via IBM SPSS software package version 20.0. Qualitative data were presented as numberds and percentage. The Kolmogorov-Smirnov test was utilized for verifying the normality of distribution. Quantitative data were presented as range (minimum & maximum), mean, SD and median. The area under the curve (AUC) evaluates the overall test performance. A 2 tailed P value < 0.05 denotes statistically significant result.

Results

Regarding demographic data, their age with a mean of 43.54 (±4.49) years. There were 38% men and 62% women. Complaint of the studied of the cases was headache in 74% of the patients, dizziness in 56% of the patients, disturbed conscious level 10% of the patients and convulsion in 70% of the patients. On reviewing conventional MRI images, the

distribution of brain tumors was supratentorial in 73% of the patients and infratentorial in 26% of the patients. The number of space-occupying lesions of the studied of the patients were solitary in 92% of the patients and multiple in 8% of the patients. The histopathological results of the brain tumors at the studied of the patients were anaplastic astrocytoma in 20%, atypical meningiomas in 8%, epidermoid cyst in 8%, glioblastoma multiform in 18%, grade IV medulloblastoma in 10% of the patients, high grade glioma in 10%, multicentric glioma in 8%, pachymeningeal metastatic lesions in 8% and pilocystic astrocytoma in 10% of the patients. Tumor grade was Grade I in 8%, grade II in 10%, grade III in 46% and grade IV in 36% of the cases. The overall tumor grading was high in 82% and low in 18% of the patients. The space-occupying lesions showed different enhancement patterns being heterogeneous in 84%, homogeneous in 8% and non-enhancing in 8% of cases. Table 1

Table 1: Demographic data, different complaints, distribution of brain tumors, number and histopathology, brain tumor WHO grading, histopathological grading of brain neoplastic lesions and enhancement pattern of the brain space-occupying lesions (n = 50)

N=50	
Age (years)	43.54 ± 4.49
Sex	
Male	31 (62%)
Female	19 (38%)
Different complaints	
Headache	37 (74%)
Convulsions	35 (70%)
Dizziness	28 (56%)
Disturbed conscious level	5 (10%)
Distribution of brain tumors	
Supratentorial	37 (73%)
Infratentorial	13 (26%)
Number of Space occupying lesions	
Solitary	46 (92%)
Multiple	4 (8%)
Histopathology of the brain space-occupying lesions	
Anaplastic astrocytoma	10 (20.00%)
Glioblastoma Multiforme	9 (18.00%)
Medulloblastoma	5 (10.00%)
High grade glioma	5 (10.00%)
Pilocytic astrocytoma	5 (10.00%)
Atypical meningoma	4 (8.00%)
Epidermoid cyst	4 (8.00%)
Pachymeningeal metastasis	4 (8.00%)
Multicentric glioma	4 (8.00%)
Grade	
Grade I	4 (8%)
Grade II	5 (10%)
Grade III	23 (46%)
Grade IV	18 (36%)
Histopathological grading	
High	41 (82%)
Low	9 (18%)
Enhancement	
Heterogeneous	42 (84%)
Homogeneous	4 (8%)
Non-enhancing	4 (8%)

Data are presented as mean ± SD or frequency (%).

No statistically significant value was determined in discriminating high- and low -grade tumor at advanced DWI and D* values analysis in the studied of the patients. The advanced ADC values were statistically insignificant between the studied brain tumors groups regarding the histopathological grading. F%, RCBV and DKI had statistically significant values in discrimination of high and low grade brain tumor in the studied cases (P value <0.001, P value <0.001, P value=0.013 respectively). Table 3

Table 3: DWI values, ADC values, diffusion coefficient D*perfusion fraction (%), relative cerebral blood volume, diffusion kurtosis imaging values (×10-3 mm2/s) in discriminating brain tumors in the studied of the patients according to tumor grading

	High grade n=41	**Low grade n=9**	**P value**
DWI (×10-3 mm2/s)	0.92 ± 0.07	0.99 ± 0.28	0.141
ADC (×10-3 mm2/s)	1.08 ± 0.55	0.96 ± 0.99	0.611
D*($\times10^{-3}$ mm2/s),	12.68 ± 2.67	11.3 ± 2.28	0.160
Perfusion fraction (%)	13.57 ± 3.58	5.1 ± 2.93	<0.001*
RCBV	8.04 ± 1.66	3.76 ± 1.96	<0.001*
DKI value	898.15 ± 407.63	500.11 ±467.92	0.013*

Data are presented as mean ± SD DWI: Diffusion weighted image. ADC: Apparent diffusion coefficient. D*: Diffusion coefficient. RCBV: Relative cerebral blood volume. DKI: Diffusion kurtosis imaging.

Perfusion fraction values showed significant elevation in high grade I comparison with in low grade brain tumors in the studied groups as well as showing marked diagnostic performance in differentiation between the high- and low-grade tumors as compared to the rest of the IVIM parameters. Table 4

Table 4: Comparative analysis of the various values of IVIM parameters of the brain tumors in studied of the patients according to tumor grading

Intravoxel Incoherent motion MRI (IVIM) parameters			
Tumor grade	**DWI Values (×10-3 mm2/ s)**	**ADC Values (×10-3 mm2/s)**	**D*(×10-3mm2/s)**
Low grade tumors	0.99 ±0.28	0.96 ±0.99	11.3±2.28
High grade tumors	0.92 ±0.07	1.08 ±0.55	14.47±4.94

Data are presented as mean ± SD DWI: Diffusion weighted image. ADC: Apparent diffusion coefficient. D*: Diffusion coefficient.

The estimated conventional DWI values used in assessment of the brain tumors in our study (P=0.041 and AUC =0.650) with 95.22% sensitivity, 80.67% specificity, 96.5% PPV and 40% NPV

The estimated conventional AD values used in assessment of the studied brain tumors in the current study (P=0.044 and AUC = 0.535) with 87.8% sensitivity, 59.56% specificity, 90% PPV and 50% NPV.

Conventional T_1 with contrast enhancement pattern of the brain tumors in the studied groups used in assessment of the brain tumors (P=0.045 and AUC=0.695) with 94.24% sensitivity, 70.44% specificity, 90.1% PPV and 50% NPV

The estimated RCBV values had a statistically significant value in assessment of brain tumors in the current study (p<0.001 and AUC=0.972) with 96.24% sensitivity, 92.89% specificity, 97.4% PPV and 66.7% NPV.

The estimated DKI values had a statistically significant value in assessment of brain tumors in our study (P=0.014 and AUC = 0.743) with 97.30% sensitivity, 94.1% specificity, 90.23% PPV and 50% NPV.

The estimated advanced DWI (IVIM parameter) values used in assessment of the brain tumors in our study (P=0.001 and AUC = 0.550) with 98.22% sensitivity, 99.23% specificity, 97.5% PPV and 50% NPV.

The estimated advanced apparent diffusion coefficient (IVIM parameter) values used in assessment of the studied brain tumors in the current study (P=0.001 and AUC=0.535) with 97.83% sensitivity, 91.24% specificity, 90% PPV and 50% NPV.

The estimated Diffusion coefficient (D*) (IVIM parameter) values used in assessment of the studied brain tumors in the current study (P=0.752 and AUC=0.556) with 89.17% sensitivity, 55.56% specificity, 91.1% PPV and 55% NPV

The estimated perfusion fraction (F %) (IVIM parameter) values had a statistically significant values in assessment of the brain tumors in our study (p<0.001 and AUC =0.985) with 99.12% sensitivity, 100% specificity, 98% PPV and 79.8% NPV. Table 5

Table 5: Role of different parameters in assessment of the brain tumors in the studied patients

Item	Sensitivity	Specificity	PPV	NPV	AUC	P value
DWI	95.22%	80.67%	96.5%	40%	0.650	0.041*
ADC	96.83%	59.56%	90%	50%	0.541	0.044*
Conventional T_1 with contrast	94.24%	70.44%	90.1%	50%	0.695	0.045*
RCBV	96.24%	92.89%	97.4%	66.7%	0.972	<0.001*
DKI	97.30%	94.1%	90.23%	50%	0.743	0.014*
Advanced DWI	98.22%	99.23%	97.5%	50%	0.550	0.001*
Advanced ADC	97.83%	91.24%	90%	50%	0.535	0.001*
Diffusion coefficient (D*)	89.17%	55.56%	91.1%	55%	0.664	0.016*
Perfusion fraction (F%)	99.12%	100%	98%	79.8%	0.985	<0.001*

DWI: Diffusion weighted image values. ADC: Apparent diffusion coefficient. RCBV: Relative cerebral blood volume. DKI: Diffusion kurtosis imaging.

The estimated DWI values couldn't predict high grade tumors in our study (P=0.357and AUC=0.650) at cut-off > 0.83 with 90.24% sensitivity, 66.67% specificity, 92.5% PPV and 60% NPV.

The estimated ADC values couldn't predict high grade tumors in the current study (P=0.836 and AUC=0.535) at cut-off > 0.69 with 87.8% sensitivity, 55.56% specificity, 90% PPV and 50% NPV. >0.69.

The estimated diffusion coefficient (D*) values couldn't predict high grade tumors in the current study (P=0.752 and AUC = 0.556) at cut-off ≤1.97 with 100% sensitivity, 55.56% specificity, 91.1% PPV and 100% NPV.

The estimated Perfusion fraction (F%) values predicted high grade brain tumors in our study (p<0.001 and AUC = 0.985) at cut-off >7.3 with 95.12% sensitivity, 100% specificity, 100% PPV and 81.8% NPV.

RCBV values significantly predicted high grade tumors in the current study (p<0.001 and AUC=0.972) at cut-off >6.2 with 90.24% sensitivity, 88.89% specificity, 97.4% PPV and 66.7% NPV.

The estimated DKI values significantly predicted high grade tumors in our study (P=0.014 and AUC=0.743) at cut-off >286 with 90.24% sensitivity, 44.44% specificity, 88.1% PPV and 50% NPV. Table 6

Table 6: Role of different parameters in prediction of high-grade brain tumors in the studied patients

Item	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	P value
DWI	>0.83	90.24%	66.67%	92.5%	60%	0.650	0.357
ADC	>0.69	87.8%	55.56%	90%	50%	0.541	0.809
Diffusion coefficient D*	>11.32	73.17%	33.33%	83.3%	21.4%	0.664	0.145
Perfusion fraction (F%)	>7.3	95.12%	100%	100%	81.8%	0.985	<0.001*
RCBV	>6.1	90.24%	88.89%	97.4%	66.7%	0.972	<0.001*
DKI	>286	90.24%	44.44%	88.1%	50%	0.743	0.014*

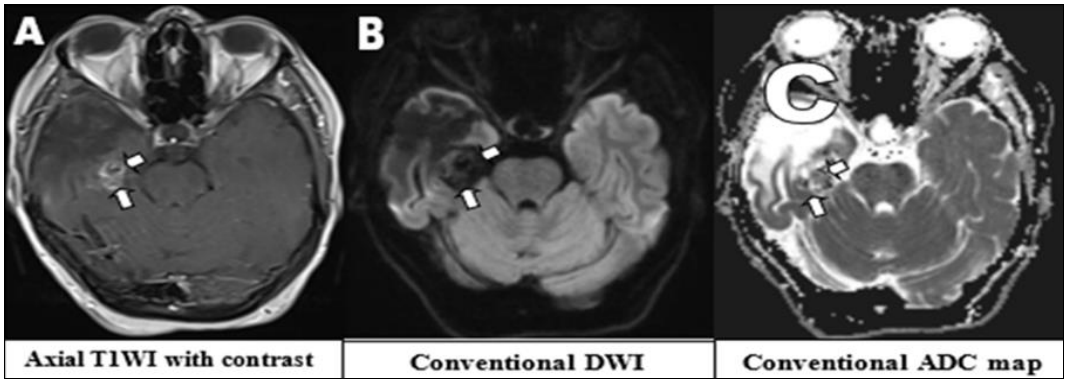
Data are presented as frequency (%). DWI: diffusion weighted image. ADC: apparent diffusion coefficient. RCBV: relative cerebral blood volume, DKI: diffusion kurtosis imaging

Case 1

A female aged 35y, presented clinically with dizziness and convulsions. Previous CT study of the brain revealed right temporal SOL measuring about 2.5 x 2.4 cm in its maximum dimensions at region and patchy cortical and subcortical area of CSF density is also seen denoting encephalomalacia. (Fig. 1).

Case 2

A female patient aged 26 y, presented clinically with headache and dizziness. (Fig. 2).



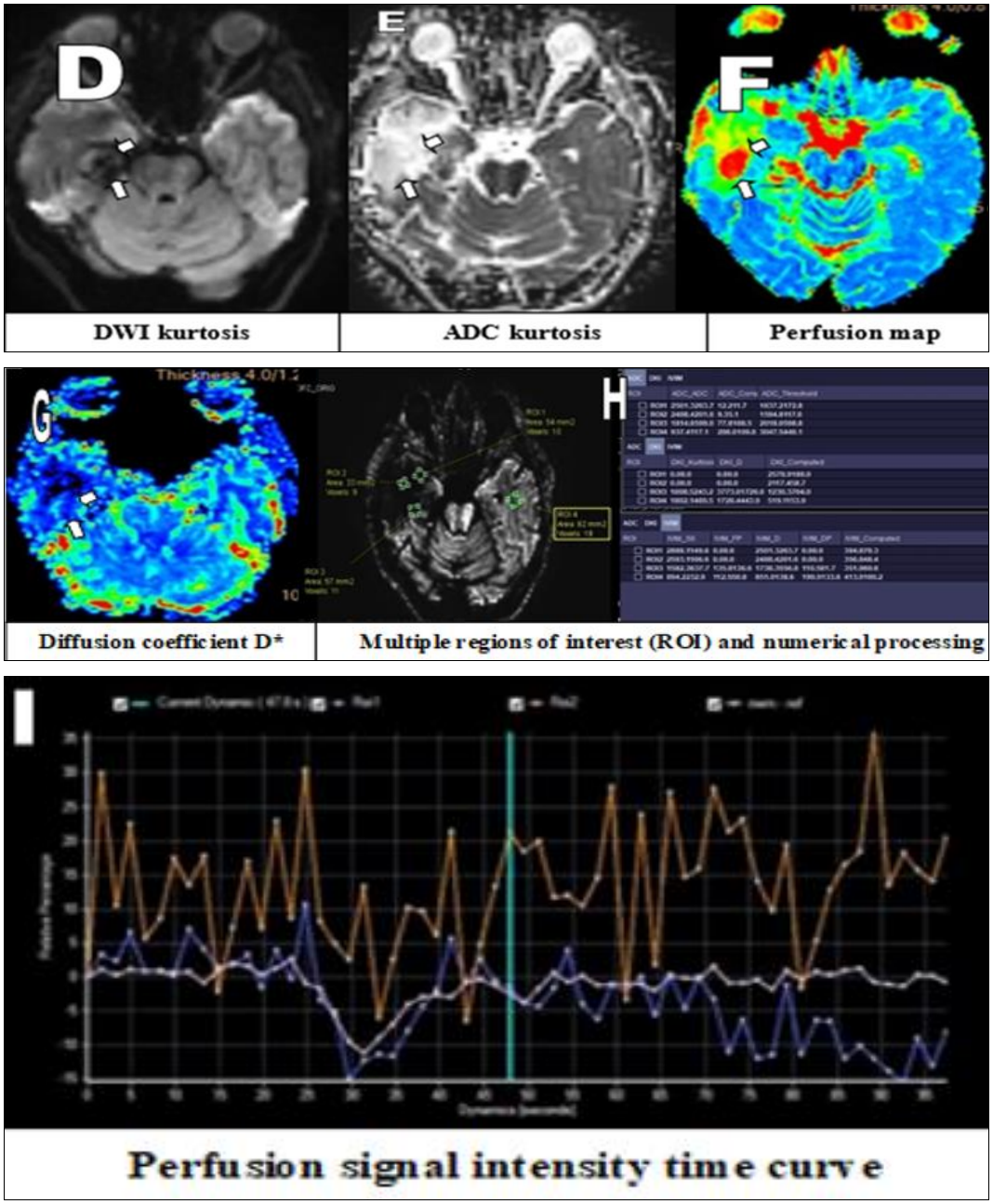
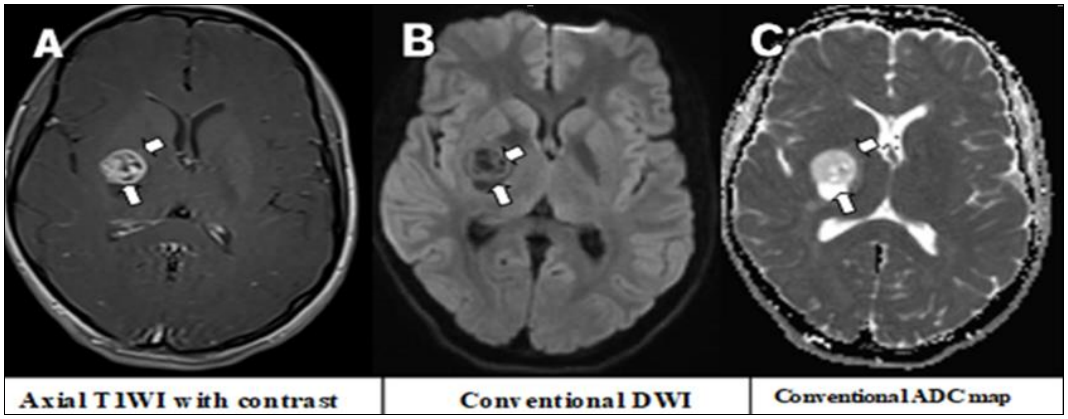


Fig 1: A heterogeneously enhancing SOL along the right temporal and right hippocampal regions (arrows in A),mild diffusion restriction with decreased ADC map (arrows in B&C),the diffusion kurtosis has highest value of 1008 with decrease in related ADC value reaching about 1.01+0.18 (×10−3 mm2/s).(arrows in D&E),mild hyperperfusion with mild elevation of various perfusion values and ratios including (the fractional perfusion of IVIM of 5.9) and rCBV is mildly elevated about 2.4 on estimated perfusion map (arrows in F), the estimated diffusion coefficient D* 11.25+11.65 (×10−3 mm2/s) (arrows in G), multiple regions of interest are taken along the lesion and normally appearing white matter with numerical processing (Dashed circle in H) and the perfusion curve pattern shows no manifest fall in SI with a relative approximation to baseline (I)



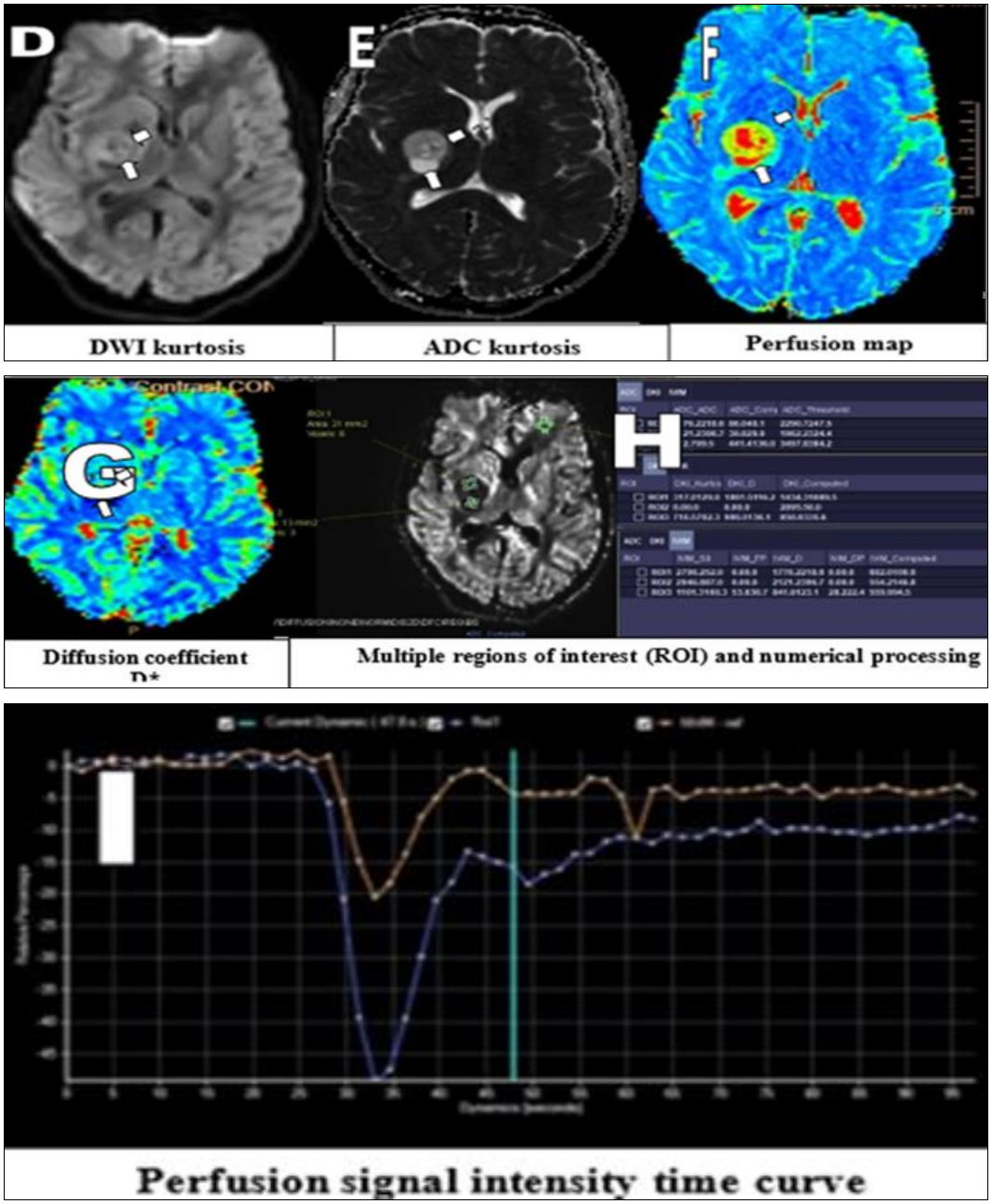


Fig 2: A non-homogenously enhancing SOL, measuring about 3.5 x 3 cm in its maximum dimensions located at the right basal ganglia (arrows in A),mild diffusion restriction with decreased estimated ADC map (arrows in B & C),the diffusion kurtosis highest value reaching about 317 with marked decrease in related ADC value reaching to 1.3+0.29 (×10-3 mm2/s) (arrows in D & E),marked hyerper-fusion with manifested abnormal elevation of various perfusion values and ratios including the fractional perfusion of IVIM (the highest value is 13.2) and rCBV is high about 8.6 on estimated perfusion map (arrows in F), the estimated diffusion coefficient D* 8.52+6. 09 (×10−3 mm2/s) (arrows in G),multiple regions of interest are taken along the lesion and normally appearing white matter with numerical processing (dashed circle in H) and the perfusion curve pattern reveals rapid steep fall in SI and tend to return to baseline (I)

Discussion

Brain tumors represent the most common primary brain tumors and they're still one of the leading causes of solid cancer-related death in individuals aged < 40 y. Gliomas is composed of a diversified broad group of neoplasms with various cell origins and diverse biological behavior. Classifying and grading of gliomas is thus critical to guide management, predict therapeutic responses and expect prognosis. Historically, the old WHO classification of gliomas depends upon the histological detection of prevailing cellular lineage and grade, mainly differentiate glioma into high-grade markedly aggressive type, and low-grade less aggressive types [9].

In the present study, grading of brain tumor was high in 41 (82%) patients and low in 9 (18%) patients. The DKI showed significant elevation in high grade in comparison with low grade (P value = 0.013). D (×10-3) was insignificantly different between both groups. D* was insignificantly different between both groups. The perfusion f was significantly higher in high grade than low grade (P value<0.001). The RCBV showed significant elevation in high grade in comparison with low grade (P value<0.001). The site was extra-axial in 17 (34%) patients and intra-axials in 33 (66%) patients. It is suggested that the decrease in RCBV determined in low grade neoplasm highly denotes a reduction in vascularity in the LGA in comparison to HGA [10].

In parallel to our result, She *et al.* [11] demonstrated the D,

and Dk value were decreased, while the K value was increased in high-grade pediatric intracranial neoplasms in comparison with low-grade type (all, P =.001).

Also, Chen *et al*. [12] who found that there was significant difference between low vs. high grade revealed for D (10−3 mm2/s) (1.4±0.4 versus 0.9±0.2, p=0.01), f (0.04±0.02 versus 0.07±0.02, p=0.02), and rCBV (2.2±0.9 vs 4.7±2.1, p=0.003). Non- significant differences were observed for D* between low versus high grades. This finding was consistent with Zhao *et al*. [13] found that the mean value of MK, Ka, Kr, and FA showed significant elevation in high GGs compared with Low GGs.

In the present study, DKI can significantly predict high grade (P = 0.014 and AUC = 0.743) at cut-off >286 with 90.24% sensitivity, 44.44% specificity, 88.1% PPV and 50% NPV.

Our result showed that, perfusion f can significantly predict high grade (p< 0.001 and AUC = 0.985) at cut-off >7.3 with 95.12% sensitivity, 100% specificity, 100% PPV and 81.8% NPV. Also, RCBV can significantly predict high grade (p< 0.001 and AUC = 0.972) at cut-off >6.2 with 90.24% sensitivity, 88.89% specificity, 97.4% PPV and 66.7% NPV.

Similar to the current study, Withey *et al*. [14] found that 40 neoplasms were categorized as low grade, forty-five as high grade. Mean whole-tumor median rCBVuncorr was more in high-grade neoplasms in comparison with low-grade ones (Mean ± SD = 2.37±2.61 vs. -0.14±5.55; p<0.01). Furthermore, Joyner *et al*. [15] found that rCBV can expect WHO grade for IDH-mutant astrocytoma. RCBV showed positive association with WHO grading (Reader A: OR 2.33 [1.35, 4.00], p = 0.002; Reader B: OR 2.13 [1.30, 3.57], p = 0.003).

This finding was consistent with She *et al*. [11] AUC of DVOI, DkVOI, and KVOI were 0.894, 0.863, and 0.885, respectively, to differentiate between high ang low-pediatric brain neoplasms. The AUC difference in grading pediatric brain neoplasms wasn't significant (all, P greater than.05). Supporting our results, Chen *et al*. [12] showed that D and f parameters from IVIM play a significant role in differentiating high from low grade pediatric intracranial neoplasm comparable to rCBV. Area under the curve from ROC was the same for all parameters of significance [D (0.81, p=0.003); f (0.80, p=0.003); rCBV (0.83, p=0.0005)].

Similarly, Zhao *et al*. [13] found that DKI and DTI are capable of significantly identifying IDH-1 mutation condition (p≦0.03). Ka (sensitivity: seventy four percent, specificity: seventy five percent, AUC: 0.72) exhibited the highest diagnostic value. The accurate cut-off value for the score was 0.76, and the corresponding sensitivity and specificity were eighty six percent and one hundred percent, respectively.

Moreover, Wang *et al*. [16]. They demonstrated that when N-MK, N-AK, and N-RK were chosen as predictive parameters of survival, the optimal cut-off values (with the highest noticed combination of sensitivity & specificity: the maximal Youden index) were 0.688 (93.75% & 76.47%), 0.825 (87.5% & 76.47%), 0.588 (81.25% and 76.47%), and 1.159 (75percent & 64.71%), respectively. The kurtosis metrics can be potentially used for predicting survival for cases having high-grade gliomas.

However, Withey *et al*. [14] found that corrected RCBV wasn't proved to be noticeably different in the studied groups. The use of a cut-off value of 0.70, the sensitivity and specificity of rCBVuncorr in Pediatric cases scanned at center 2 were one hundred percent; for rCBVcorr, they become lower reaching seventy one percent and eighty percent, respectively, with a cut-off of 1.15; for K2, one hundred percent sensitivity and specificity were obtained with the use of a cut-off of 0.005.

In the current study, DWI can't predict high grade (P =0.357 and AUC = 0.650) at cut-off >0.83 with 90.24% sensitivity, 66.67% specificity, 92.5% PPV and 60% NPV. Also, ADC can't predict high grade (P =0.836 and AUC = 0.535) at cut-off >0.69 with 87.8% sensitivity, 55.56% specificity, 90% PPV and 50% NPV. Microscopic necrotic foci in atypical/malignant neoplasm might lead to more H_2O diffusion, enhancing the ADC value of the high grade tumors. The existence of microscopic neurotic foci was determined in the pathological slide of a single case of cases included in this study without evidence of gross necrotic lesions on the MRI [17]. These findings are the most significant factor hindering grade evaluation with DWI.

In agreement with our study, Haghighatkhah and Yousef *et al*. [18] The ADC value in intra-tumoral and peri-tumoral regions of the intracranial tumor metastatic lesion might not predict the assessment of morphology or the origin of the neoplasm.

Supporting our results, Sanverdi *et al*. [19] found that DW MR imaging hasn't any extra value in the determination of the histologic behavior or in the differentiation histopathological types of meningiomas.

In disagreement with our results, Mokhtar *et al*. [20] found that Adding DWI and ADC values to the conventional MRI assessment of the brain enhances the diagnostic precision of predicting the pediatric brain tumors histopathological grading. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of DWI in differentiation between high and low grade brain neoplasm were eighty nine percent, one hundred percent,one hundred percent, eighty six percent and ninety -three percent respectively. This difference may be because of different sample sizes.

In the present study, diffusion coefficient D* values can't predict high grade (P =0.752 and AUC = 0.556) at cut-off ≤1.97 with 100% sensitivity, 55.56% specificity, 91.1% PPV and 100% NPV. The same as the current work, Chen *et al*. [12] found that diffusion coefficient D* values can't clearly determine high vs. low grade pediatric intracranial neoplasm.

In the current study, enhancement can significantly predict high grade (P =0.045 and AUC = 0.695) with 90.24% sensitivity, 44.44% specificity, 88.1% PPV and 50% NPV.

Similar to the present study, Bai *et al*. [21] demonstrated that H_2O molecular diffusion heterogeneity index and MK values could give more data and enhance the grading of glioma tumor in compared with traditional diffusion parameters. Supporting our results, Guo *et al*. [22] found that E dynamic contrast-enhanced MRI can significantly predict high grade brain tumor.

However, Chen *et al*. [12] found that dynamic contrast enhancement parameters can't clearly differentiate high vs. low grade pediatric intracranial neoplasms. This difference may be because of different sample sizes.

In our study, we faced some limitations as: the sample size is considered relatively small, selecting an area of interest to assess the rCBV causes another obstacle in cases that the tumor was located within gray matter as it's not clear if the high perfusion value results from the criteria of the gray

matter itself or because of the neoplasm, another obstacle in the study was the absence of a multi-parametric analysis that might reveal the relative participation of all the clinical, traditional MRI and advanced finding to the diagnosis of LGA compared to HGA and The areas of interest were chosen in the solid portions of the tumor alternative to the whole gliomas in the current work, thus could help to select bias according to the histological heterogeneity of gliomas.

Conclusions

DKI at cut-off >286, Perfusion fraction at cutoff >7.3, RCBV at cutoff > 6.2 and diffusion enhancement can significantly predict high grades of BTs ($p< 0.05$). However, DWI, ADC, and diffusion coefficient D* can't predict high grade of BTs ($p< 0.05$).

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Conflict of Interest

Nil

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