

# A Retrospective Analysis of ADC values with HPE Correlation in Grading of Brain Tumours

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## A B S T R A C T

**Introduction:** The gold-standard for brain tumor diagnosis is light microscopy analysis of histological tissue samples. DWI have been used to study various diseases. Our hypothesis is that DWI and tumour ADCs provide additional information in diagnosis of patients with brain tumours. MR diffusion imaging provides an intriguing access to information that otherwise can only be obtained by invasive light microscopy.

**Material and methods:** 50 patients with histologically verified brain tumours who underwent conventional MRI, DWI, CEMR and proton MR Spectroscopy were analyzed. We defined tumour as an area containing highest Ch/ Cr and Ch/NAA Ratios, contrast enhancement and abnormal T2W signal intensity. Normal brain tissue had normal proton MR spectra, no enhancement and normal T2 signal intensity. ADC maps were calculated and ROI were manually placed over areas of tumour and normal tissue.

**Results:** The ADCs of anaplastic astrocytomas were lower than those of low grade astrocytomas; The ADCs of medulloblastomas were lower than high grade astrocytomas. Meningiomas had a wide range of ADC values.

**Conclusion:** ADCs when combined with conventional MR findings are better predictors of degree of malignancy as ADCs correlated well with tumour cellularity.

**Keywords:** ADC, DWI, Brain Tumour

## INTRODUCTION

MR diffusion imaging has been used to study various diseases and normal brain parenchyma. The development of techniques capable of accurately depicting tumour grades in vivo is important for determination of the most appropriate treatment for glioma.<sup>1</sup>

The gold standard for brain tumour diagnosis is light microscopy analysis of histological tissue samples.<sup>2</sup> MR diffusion imaging probes water molecular diffusion over distances that correspond to typical cell sizes and this water diffusion is also impeded by membranes, i.e., structures that are an integral part of the cell architecture. With increasing cell density, the impeding effect of membranes is expected to increase. Thus, MR diffusion imaging provides an intriguing access to information that otherwise can only be obtained by invasive light microscopy. In malignant gliomas, peritumoral edema, which can be depicted with either CT or MRI, often has been reported to have infiltrating neoplastic cells.<sup>3</sup> Therefore, the tumor border is still inaccurately depicted even with imaging techniques. Our initial observations of astrocytic tumors revealed a relatively good correlation between ADC and tumor cellularity. We sought to determine whether ADC

values are more useful than conventional MR images in differentiating tumor, edema and normal brain tissue.

## MATERIAL AND METHODS

50 patients (34 women and 16 men, 12-65 years old) with histologically proven brain tumours who underwent MRI on 1.5-T Siemens MR unit (Avanto) in our hospital over a period of two years were analyzed

### MRI Protocol Included

Axial FSE FLAIR, T2W, T1W, GRE sequences, sagittal T1W, T2W sequences, contrast enhanced axial, coronal, and sagittal T1W sequences, MR spectroscopy were acquired. DWI with ADC maps were acquired using b values of 0, 500, and 1000 s/mm<sup>2</sup> applied in the X, Y, and Z directions. For each lesion, we defined the following regions on the basis of imaging features:

**Tumor-** Highest Cho/Cr and Cho/NAA ratios, contrast enhancement, and abnormal T2W signal intensity;

**Edema** - Normal Cho/Cr and Cho/NAA ratios, no enhancement, and high T2W signal intensity; and

**Normal tissue** - Normal Cho/Cr and Cho/NAA ratios, no

Tumours	Extra/Intraaxial	PLAIN T2W	T1+C Enhancement	Oedema	MRS	ADC / MEAN ADC	WHO Grade
Pilocytic Astrocytoma	Intraaxial	Hyperintense, With Solid Component	Enhancing Solid Nodule	-	↑Ch/Cr	1849-2130 (2025)	I
Haemangioblastoma	Intraaxial	Hyperintense With Peripheral Solid Nodule	Enhancing Solid Nodule	-	↑Ch/Cr	1390-1645 (1450)	I
Grade 2 Astrocytomas	Intraaxial	Hyperintense Solid Cystic Lesion	Patchy	Minimal	-	1450-1657 (1657)	II
Oligodendroglioma	Intraaxial	Hyperintense Lesion With Signal Loss Areas	Heterogenous	-	-	1370-1506 (1425)	II
Anaplastic Astrocytoma	Intraaxial	Hyperintense Lesion	Intense With Central Necrotic Areas	+	↑Ch/Cr	997-1257 (1040)	III
Glioblastoma	Intraaxial	Hyperintense Lesion Crossing Midline	Thick Nodular Ring	+	↑Ch/Cr	780-978 (850)	IV
Medulloblastoma	Intraaxial	Hyperintense Lesion In Posterior Fossa	Heterogenous & Intense	+	↑Ch/Cr	670-800 (740)	IV
Anaplastic Oligodendroglioma	Intraaxial	Hyperintense Lesion	Intense	+	↑Ch/Cr	1101-1245 (1190)	III
Meningioma	Extraxial	Isointense Lesion	Homogenous	-	-	678-1705 (1191)	
Pituitary Adenoma	Extraxial	Sellar Mass With Cystic Areas	Dynamic	-	-	1060-1240 (1130)	
Admantomatous craniopharyngioma	Extraxial	Hyperintense Suprasellar Mass	No	-	-	2120-2600 (2420)	
Metastasis	Intraaxial	Multiple Isointense Lesions	Ring Like	+	↑Ch/Cr	710-900 (800)	

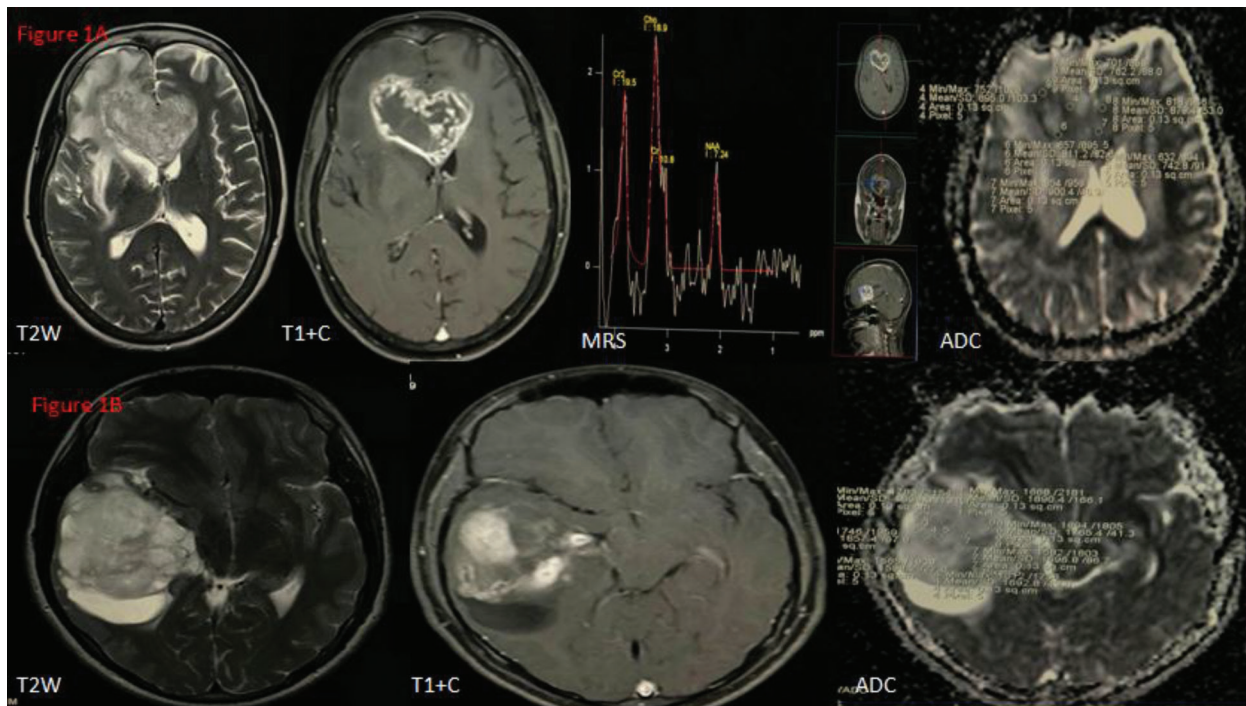
Table-1:

enhancement, and normal T2W signal intensity. We then manually selected a region of interest (ROI) on the ADC maps corresponding as closely as possible in location and size to the three (or four) regions previously described. In patients who had low grade tumours with poor enhancement,

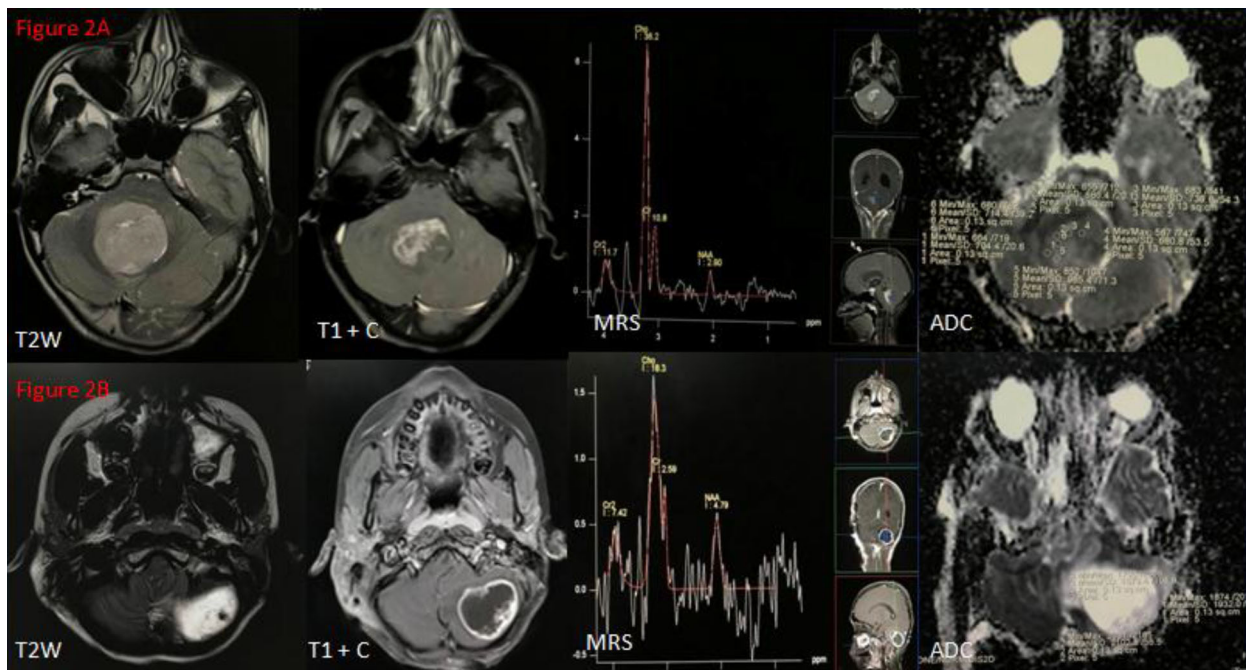
ROIs were chosen after identifying the tumour area on T2W and T2W images.

## RESULTS

In the present study conducted in our hospital over a period



**Figure-1(A):** showing 50 year old female with seizures: T2W- Isointense lesion in b/l frontal lobes crossing midline with edema; T1+C -Thick nodular ring enhancement, MRS-Cho/Cr Elevated, MEAN ADC-788(Low); HPE-Glioblastoma. **Figure-1(B):** Showing 16 year old male with seizures: T2W- Hyperintense lesion with solid cystic component in right temporal lobe; Contrast T1W - Patchy enhancement in solid part; MEAN ADC-1657 (Mildly High); HPE - Astrocytoma Grade II.



**Figure-2(A):** 15 year old female with ataxia, headache; T2W- Hyperintense Lesion in posterior fossa in midline 4th ventricle; T1+C -Heterogenous intense enhancement, MRS-Cho/Cr Elevated, MEAN ADC-730(Low); HPE- Medulloblastoma; **Figure-2(B):** T2W-Cystic Lesion in left cerebellar hemisphere with peripheral solid component with areas of signal loss; T1+C-Enhancement of solid part and peripheral rim; MRS- Elevated Ch/Cr; ADC -2025(High); HPE-Pilocytic Astrocytoma

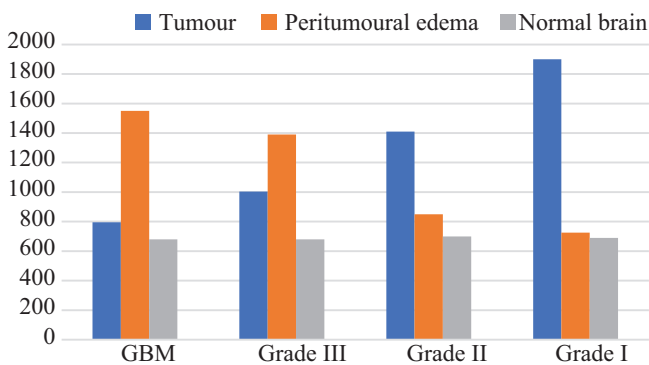


Figure-3:

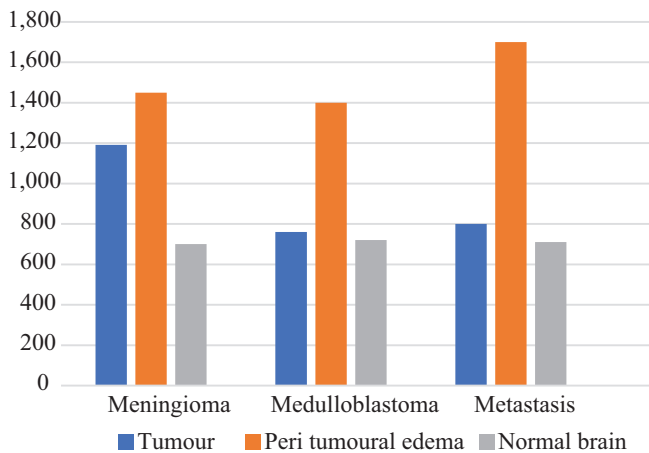


Figure-4:

of two years, peak age group was 40-55 years. Of the 50 patients, females comprised the majority 34 cases (68%) followed by males 16 cases (32%). Seizures was the most common presenting symptom in 35 patients (70%). Extra-axial tumors accounted for 12 cases (24%) and intra-axial tumors accounted for 38 cases (76%). Gliomas accounted for 16 cases (32%) followed by meningiomas 8 (16%). Out of 50 patients, lesions were distributed mostly in frontal region in 15 cases followed by parietal regions in 10 cases. Lesions were heterogeneously hyperintense on T2W in 17 cases. Mass effect was seen in 36 cases (72%). On contrast administration there was homogeneous enhancement in 14 cases (28%) comprising mainly of meningiomas (8 cases). The ADCs of the tumors are shown in below Table-1. They ranged between 1849-2130 for pilocytic astrocytomas, 1450-1657 in grade 2 astrocytomas, 997-1257 in anaplastic astrocytomas, and 780 -978 in GBMs. In sellar and suprasellar lesions they ranged between 1060-1240 in pituitary adenoma and between 2120-2600 in adamantinomatous craniopharyngioma. They ranged between 670-800 in medulloblastoma. Meningiomas showed wide variation in their ADC values ranging between 678-1705. In metastatic tumours they ranged between 710-900. Evaluation of spectroscopy was possible in only 43 cases and was not performed in 7 cases because of presence of the lesion close to the bone. Elevated choline/creatinine ratio was observed in enhancing tumour area.

## DISCUSSION

MR diffusion imaging has been used to study water mobility

in normal brain tissue, cerebral infarction, multiple sclerosis, gliomas and brain abscesses and to differentiate between arachnoid cysts and epidermoid cysts and other diseases.<sup>1</sup> The present study was a retrospective study aimed at studying MR appearances and ADC values of different brain tumours. Gliomas are the most common brain tumours. Malignant gliomas usually enhance after intravenous contrast injection and show peritumoral edema, whereas, low grade gliomas usually show little to no abnormal enhancement or peritumoral edema. Our study shows that lower ADCs suggest malignant glioma, where as higher ADCs suggest low-grade astrocytoma (Figure 1A , 1B ). These results agree with those of previous reports<sup>1,2,3</sup> enhancing tumor had the lowest ADC values and cyst/necrotic tumor the highest.

On the basis of specific histologic features of the tumour, such as cellularity, nuclear atypia, mitosis, pleomorphism, vascular hyperplasia, and necrosis.<sup>4</sup> Of these features, tumour cellularity is the main correlate of quantitative assessment with DWI. With increasing cell density as seen with increasing grade of tumours, the impeding effects of cellular membranes and reduced intracellular and extracellular fluid are expected to result in low values of ADC in high grade tumours and high values of ADC in low-grade tumours. In short, the ADC value of an astrocytoma may aid conventional MRI in characterizing the tumour and therefore help to plan treatment and assess prognosis accordingly. Because the majority of the translational movement of water occurs in the extracellular space, swelling or increased cellularity should affect the ADC. Thus, the lowest ADC value should indicate the region of greatest cellularity and be helpful in selecting biopsy targets. In our study lowest ADC values favoured high grade tumours; and high ADC values favoured low grade; this finding also correlated with study by Aneela-Darbar and Muhammad Waqas.<sup>5</sup>

Proton MR spectroscopy findings seem to indicate that there is a correlation between ADC and levels of choline in tumours. In our study the areas showing low ADC values had increased choline/creatinine ratio. Gupta et al<sup>6</sup> also studied 20 tumors with proton MR spectroscopy and ADC maps and found that areas of dense hypercellular tumor showed increased choline and low ADC which is similar to our findings.

Diffusion measurements have also been used to study tumor response to treatment. In an animal model of glioma, tumors that were treated with chemotherapy showed increasing ADC values 6 to 8 days after treatment, probably corresponding to acute necrosis and a loosening of the extracellular space.<sup>7</sup> In the presence of tumor regrowth, ADC values again dropped and returned to pre-treatment levels. Therefore, ADC maps may have some utility for monitoring response to tumor treatment—an observation that needs to be tested in humans. In Stephen and Robert Study<sup>2</sup> of diffusion imaging of brain tumours, diffusion-based fiber tract localization is performed during treatment planning. The application of diffusion imaging with an Extended B-factor range shows some interesting potential for diagnostic imaging in brain tumours and improved detection of crossing nerve fiber tracts.<sup>2</sup>

Tien et al<sup>8</sup> could distinguish areas of peritumoral, neoplastic cell infiltration from predominantly peritumoral edema

when abnormalities were located in the white matter aligned in the direction of the diffusion-weighted gradient. Our findings do not support the hypothesis that peritumoral neoplastic cell infiltration can be depicted by ADC Maps. In a study by Abdulaziz and Hussain<sup>9</sup> on paediatric brain tumours, pilocytic astrocytomas have significantly higher average ADC values than those of ependymomas and medulloblastomas; our study has shown similar results (Fig 2A, 2B).

In sellar and suprasellar tumours we observed that craniopharyngiomas had higher ADC values than pituitary macroadenomas. Metastatic tumours had low ADC values while meningiomas had wide variation in range of their ADC values. In a study by Yamasaki and Kirusu<sup>10</sup> ADC was useful for differentiation of some human brain tumors, particularly Malignant Lymphomas versus Glioblastomas and Metastatic Tumors, and Ependymomas versus PNETs. In our study we could differentiate PNETs from glioblastomas; and between pilocytic astrocytomas and medulloblastoma. In a study by Maria Zulfaiker and Hong Lai<sup>4</sup>, low ADC values, independent of tumor grade, correlated with poor survival in malignant astrocytomas.

Because of the varying results reported in the literature, we decided to evaluate 50 brain tumours with ADC mapping and proton MR Spectroscopy. We did not seek to establish which technique is best but solely to test the hypothesis that ADC values can differentiate tumour, edema, and normal brain and in utility of ADC in tumour grading (Figure 3, 4). In Our study, the values ranged between 1849-2130 for pilocytic astrocytomas, 1450-1657 in grade 2 astrocytomas, 997-1257 in anaplastic astrocytomas, and 780 - 978 in Glioblastomas. We found that ADC values cannot be used in individual cases to differentiate tumor types reliably. Although the ADC's of grade II astrocytoma and glioblastoma overlapped in some cases (4%), the combination of routine image interpretation and ADC had a higher predictive value. Our results indicate that lower ADCs suggest malignant glioma, where as higher ADCs suggest low-grade astrocytoma. These results agree with those of previous studies. The ADC was not useful for differentiating one type of meningioma from another.

## CONCLUSION

In conclusion, ADC values among patients with astrocytic tumors, those with glioblastoma had lower ADC values than those with grade II astrocytoma. The values in pilocytic astrocytoma/ haemangioblastoma > grade II astrocytomas > anaplastic astrocytomas > glioblastomas > medulloblastoma. The ADC did not differ significantly between patients with glioblastomas versus metastatic tumors. Patients with meningiomas had a wide range of ADC values. We do not support the hypothesis that peritumoral neoplastic cell infiltration can be depicted by ADCS.

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