

# Minimum apparent diffusion coefficient (ADC) value in differentiation of high and low grade gliomas, does it make a difference?

## Abstract

**Objectives:** This study aimed to study the minimum and mean ADC values in the differentiation of high and low grade gliomas.

**Background:** Diffusion-weighted imaging (DWI) has greatly enhanced the ability of MRI to differentiate high and low grade gliomas where the ADC values inversely correlated with the tumor grade.

**Methods:** This retrospective study included 50 patients (M/F 23/27) with pathologically proven gliomas (30 patients with high grade and 20 with low grade gliomas) who underwent MRI with diffusion weighted sequence (b-value 1000s/mm<sup>2</sup>) acquired on a 1.5T scanner at menoufia university hospital.

**Results:** Diffusion restriction was found in 93.3% of cases of high grade gliomas (n=28/30) with mean calculated ADC value of calculated mean and minimum ADC values were  $0.87 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $0.82 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{sec}$  respectively. In low grade gliomas diffusion restriction was identified in 7 cases (n=7/20, 35%) with a mean calculated ADC values of  $1.3 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $1.15 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{sec}$  for the mean and minimum ADC respectively. Statistical significance was found between the calculated ADC values of the high and low grade gliomas when using the minimum and mean ADC values between the high and low grade gliomas (p value <0.001)

**Conclusion:** We have demonstrated that both mean and minimum ADC values measurements can be used when trying to differentiate high and low grade gliomas with both showing statistical significance.

**Keywords:** DWI, gliomas, grade, MRI, ADC, ischaemic infarctions, vasculopathies, neoplasms, peritumoral edema

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**Abbreviations:** DWI, diffusion weighted image; MRI, magnetic resonance image; ADC, apparent diffusion coefficient; T, tesla; FOV, field of view; ROI, region of interest

## Introduction

Diffusion weighted imaging (DWI) is a relatively new method. It was introduced in clinical practice in 1990's; initially much of its role was described in acute ischaemic stroke.<sup>1,2</sup> It provides information about physiologic state of the brain and is particularly sensitive for ischaemic infarctions.<sup>3</sup> It provides image contrast that is dependent on the molecular motion of water, which may be substantially altered by disease.<sup>2</sup>

This technique exploits the phenomenon of diffusion, which is related to Brownian motion at the molecular level. DWI takes advantage of the fact that intracellular water molecules are much more limited in their movement than extracellular ones, because they quickly bump into the cell membrane that contains them. The more restricted the movement of water, the brighter it will be on DWI sequences.<sup>4</sup> DWI consists of a DW image, also called the diffusion trace, and an apparent diffusion coefficient (ADC) map. DW image is a T2-weighted echoplanar background image attenuated by the rate of apparent diffusion. DW image, together with qualitative and quantitative assessment of the ADC map has been widely used in the diagnosis of acute cerebral infarction, owing to the reliable distinction

of cytotoxic and vasogenic edema.<sup>2</sup> DWI is highly sensitive in detecting early cerebral ischemic changes in acute stroke patients.<sup>5</sup>

DWI has very recently been described and suggested in the differential diagnosis of various non-infarct lesions of the brain which are hyperintense in the diffusion trace image, such as infectious, neoplastic and demyelinating diseases, encephalopathies, leukodystrophies, vasculitis and vasculopathies, hemorrhage and trauma.<sup>6</sup> Gliomas are the most common primary neoplasms of the brain in adults ranging in grade from low to high.<sup>7</sup> Glioma grading is based on the histopathologic assessment of the tumor and is critical for planning therapeutic approaches and assessing prognosis and response to therapy.<sup>8</sup> Advanced MR imaging techniques such as DWI provide physiologic information that complements the anatomic information obtained from conventional MR imaging.<sup>9,10</sup>

The signal intensity of gliomas on DW images is variable (hyper-iso-, or hypointense).<sup>11</sup> Glioma grade correlates inversely with minimum ADC values that can be explained on the basis of increasing tumor cellularity with grade.<sup>12</sup> Tumors with higher cellularity or higher grade show increased signal on the DW image and a marked reduction in ADC values; In addition to the hypercellularity which causes increased intracellular water, the low ADC values are also related to the decreased extracellular fluid. Low grade gliomas, because of their low cellularity, have a significantly higher ADC values compared to high grade gliomas.<sup>13</sup>

Measurement of ADC values should be done from the maximally restricted diffusion areas, because histologically the actual grade of the tumor is determined from the areas with the highest grade. DWI can provide information about peritumoral neoplastic cell infiltration, perhaps even help discriminate the boundaries between tumor, infiltrating tumor, peritumoral edema, and normal brain parenchyma.<sup>14</sup> The aim of this study was to evaluate the diagnostic accuracy of DWI and ADC calculation in the characterization of the grade of different gliomas. Our objectives were the following: 1) to evaluate the diffusion characteristics in high and low grade gliomas, 2) to establish whether there is any difference in the calculated ADC values in gliomas grading, 3) to investigate whether the use of minimum ADC values improve the diagnostic accuracy of DW MR imaging.

## Patients and methods

### Study Population

We retrospectively reviewed data obtained from 50 patients with a histopathologically proved diagnosis of gliomas (30 patients with high grade and 20 patients with low grade gliomas) who underwent an MR imaging study at our department (menoufia university hospital, MRI unit) from January 2013 till January 2015. Diagnoses were histologically confirmed by surgical resection or biopsy.

### Magnetic resonance imaging

All of the patients underwent MR imaging study on a 1.5 T clinical scanner (Toshiba Vantage) using standard head coil (NV SPDR) with 240x240-mm FOV. Conventional MR images consisted of axial T1WI, axial T2WI, axial FLAIR, sagittal T1WI, coronal T2WI and contrast-enhanced images T1-weighted images after intravenous contrast injection (gadopentetate dimeglumine, 0.1mmol/kg). DW MR imaging was acquired in the axial plane by using a single-shot, spin-echo echo-planar imaging sequence (with b-values of 1000second/mm<sup>2</sup>) in 3 orthogonal directions.

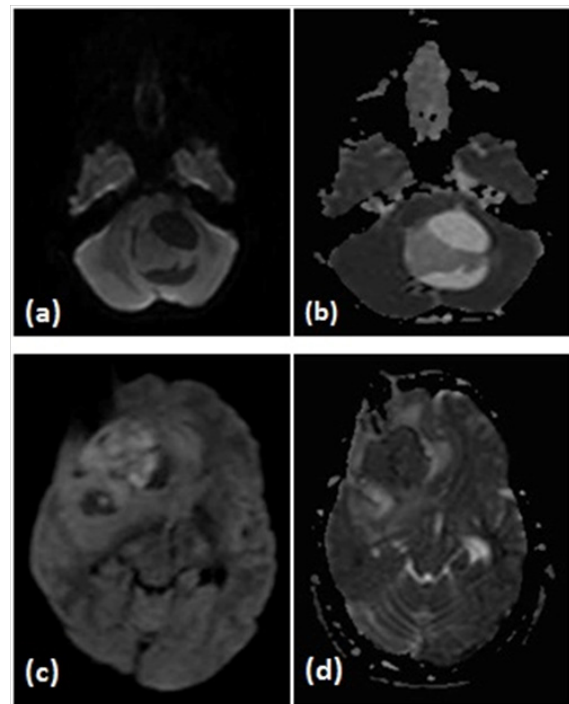
### DWI data analysis

Isotropic (trace, i.e, the summation of 3 orthogonal directions) DW images & ADC maps were visually inspected and classified as restricted and free diffusion compared with normal white matter. ADC maps and values were calculated by using the inbuilt manufacturer's software with the ROIs. ROIs were manually constructed and placed over the region of the maximum hypointensity corresponding to the highest diffusion restriction of the solid portion of tumor, Figure 1. Afterward, the minimum and mean ADC obtained was selected for the analysis. Control ADC values were obtained from normal-appearing white matter on the normal brain tissue unaffected by pathology. ROIs values were expressed as 10<sup>-3</sup>mm<sup>2</sup>/s. The ROIs were carefully placed to avoid cystic, necrotic, and hemorrhagic regions that might influence ADC values. Both values were compared using the 2-sample t test with statistical significance set at P<0.05. Minimum and mean ADC values of both low and high grade gliomas were also compared together using U test with statistical significance set at P<0.001.

## Results

### Patient population

The studied group consisted of 50 patients (23 males and 27 females) with ages ranging from 7 to 77years with a mean age of 36.4years. the age and gender distribution is summarized at Table 1, that shows low grade gliomas to be more common in those under the age of 20 years (n=13/20, 65%), while high grade glioma was commoner in those aged >30-50years (n=15/30, 50%).

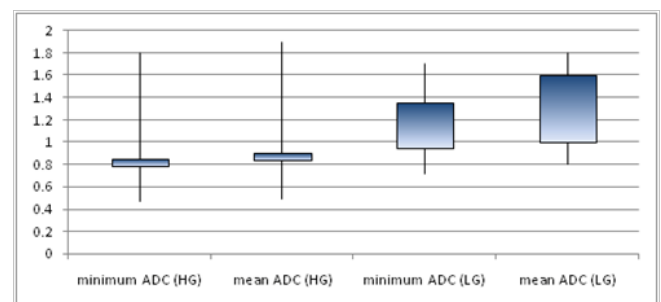


**Figure 1a & 1b** Axial isotropic DWI and ADC map of a pilocytic astrocytoma showing no diffusion restriction of the solid part of the tumor.

**Figure 1c & 1d** axial isotropic DWI and ADC map of a right frontal lobe glioblastoma multiform showing diffusion restriction.

**Table 1** The demographics of the study

Age in years	High grade glioma N=30		Low grade glioma N=20	
	Male	Female	Male	Female
0- 10	-	-	3	3
>10-20	2	-	3	4
> 20- 30	3	-	-	2
>30-40	3	4	-	-
>40-50	2	6	3	1
>50- 60	-	4	-	1
>60-70	2	1		
>70	2	1		
Total	14	16	9	11



**Figure 2** Boxplots showing the range of minimum and mean ADC values encountered in the studied 30 high grade and 20 low grade gliomas.

HG, high grade gliomas; LG, low grade gliomas

## Diffusion characteristics and ADC value analysis

Diffusion restriction was found in 93.3% of cases of high grade gliomas (n=28/30) with mean calculated ADC value of calculated mean and minimum ADC values were  $0.87 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $0.82 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{sec}$  respectively. In low grade gliomas diffusion restriction was identified in 7 cases (n=7/20, 35%) with a mean calculated ADC values of  $1.3 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $1.15 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{sec}$  for the mean and minimum ADC respectively. Statistical significance was found between the calculated ADC values of the high

and low grade gliomas and those of the NAWM in the same patients. These findings are summarized in Table 2 & Figure 2.

Table 2 summarizes the diffusion characteristics of the studied high and low grade gliomas with the mean calculated ADC values in comparison to those of the normal appearing white matter in the same patients. Statistical significance was also found between the calculated minimum and mean ADC values between the high and low grade gliomas (p value <0.001), Table 3.

**Table 2** The ADC values

	True restriction		Mean ADC value $\pm$ SD	ADC value $\pm$ SD of	Min. ADC value $\pm$ SD	P
	No.	%	( $\times 10^{-3} \text{ mm}^2/\text{sec}$ )	NAWM ( $\times 10^{-3} \text{ mm}^2/\text{sec}$ )	( $\times 10^{-3} \text{ mm}^2/\text{sec}$ )	value
High grade gliomas	28/30	93.30%	$0.87 \pm 0.3$	$0.67 \pm 0.04$	$0.82 \pm 0.3$	<0.05
Low grade gliomas	7/20	35%	$1.3 \pm 0.3$	$0.73 \pm 0.07$	$1.15 \pm 0.2$	<0.05

ADC, apparent diffusion coefficient; Min, minimum; No, number; SD, standard deviation

**Table 3** Comparison of the ADC values in the studied high and low grade gliomas

	High grade glioma N=30		Low grade glioma N=20	
ADC	( $\times 10^{-3} \text{ mm}^2/\text{sec}$ )		( $\times 10^{-3} \text{ mm}^2/\text{sec}$ )	U test P value
Min	$0.82 \pm 0.3$		$1.15 \pm 0.28$	3.77 <0.001
Mean	$0.87 \pm 0.3$		$1.3 \pm 0.3$	4.3 <0.001

The table shows the statistical significance found between the minimum and mean ADC values of high and low grade gliomas.

ADC, apparent diffusion coefficient; Min, minimum; N, number

## Discussion

Gliomas are the most encountered intra-axial brain neoplasm, hence accurate grading of gliomas is of utmost importance because the therapeutic approach and prognosis differ considerably according to tumor grade.<sup>9,15,16</sup> Conventional MR imaging provides information on contrast enhancement, mass effect, edema, and necrosis, however it is not always accurate for the precise grading of glioma. Advanced MR imaging techniques such as perfusion and diffusion MR imaging have demonstrated great utility for the assessment of brain tumors.<sup>9</sup>

Diffusion-weighted magnetic resonance (MR) imaging provides image contrast that is different from that provided by the conventional MR techniques<sup>12</sup> as DWI allows assessing the cellularity of tumors in a noninvasive form. As cellular and subcellular elements impede water mobility,<sup>16</sup> hence quantitative information from the restriction of water molecule movement can be observed in calculating the ADC.<sup>13,17,18</sup> Thus, brain neoplasms with higher cellularity or with a higher grade show a significant reduction in ADC values.<sup>18</sup>

In our series of 50 gliomas, lower ADC values were identified at high grade gliomas, n=30 ( $0.87 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  for mean ADC value) compared to low grade gliomas, n=20 ( $1.3 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  for mean ADC value). This goes with the findings found by Bulakbasi et al.,<sup>19</sup> who studied 8 cases of low grade gliomas and 12 cases of high grade gliomas and showed lower ADC values in high grade gliomas than in low grade gliomas (mean ADC values of  $0.87 \pm 0.1 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $1.15 \pm 0.116 \times 10^{-3} \text{ mm}^2/\text{sec}$  respectively).

When using the minimum ADC values also significant difference was identified between high and low grade gliomas with measured values of  $0.82 \pm 0.3 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $1.15 \pm 0.28 \times 10^{-3} \text{ mm}^2/\text{sec}$  respectively. This goes with that found by Hilario et al.,<sup>15</sup> who studied the minimum ADC values of 162 gliomas. Their measures were  $0.78 \pm 0.18 \times 10^{-3} \text{ mm}^2/\text{sec}$  and  $1.27 \pm 0.29 \times 10^{-3} \text{ mm}^2/\text{sec}$  for high and

low grade gliomas respectively. The difference in numbers is probably attributed to the smaller studied group in our study (n=50).

Similar findings were also reported by previous, however in a smaller study population, Lee et al.,<sup>17</sup> (n=16), Kwee et al.,<sup>20</sup> (n=17), and Calli et al.,<sup>18</sup> (n=31), Also demonstrated increased signal intensity on DWI in high grade gliomas with significant reduction in their ADC values. Our findings also agree with those by Yamasaki et al.,<sup>21</sup> who demonstrated significant reduction in ADC values when comparing low grade gliomas versus high grade gliomas.

## Conclusion

Our results in a series of 50 patients with gliomas confirmed that DWI with ADC value measurements can be used to differentiate high and low grade gliomas in a noninvasive method for approximating tumor grade. We have demonstrated that both mean and minimum ADC values measurements can be used when trying to differentiate high and low grade gliomas with both showing statistical significance.

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## Conflicts of interest

Author declares there are no conflicts of interest.

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