

## Whole Tumor Volume Based Histogram Analysis of ADC for Differentiating between who Grade II and III Glioma

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## 1. Introduction

The therapeutic approaches and prognosis for gliomas differ considerably for different tumor grades, it is hence important to accurately assess glioma grade for treatment planning. In addition to the use of conventional mean value, several studies have reported the use of histogram analysis of ADC in glioma grading [1,2]. However only the differentiation between low grade and high grade was concerned, whereas differentiation between grade II and III remains challenging. A limitation in previous studies could be the use of multiple ROIs in a section of the tumor lesion, which may underestimate the heterogeneity of glioma cellularity. In this study, the differential diagnostic value of histogram analysis of ADC signal value based on entire region of grade II and III tumor is investigated, and further aimed at revealing the microscopic changes of glioma in the evolution of low grade to high grade.

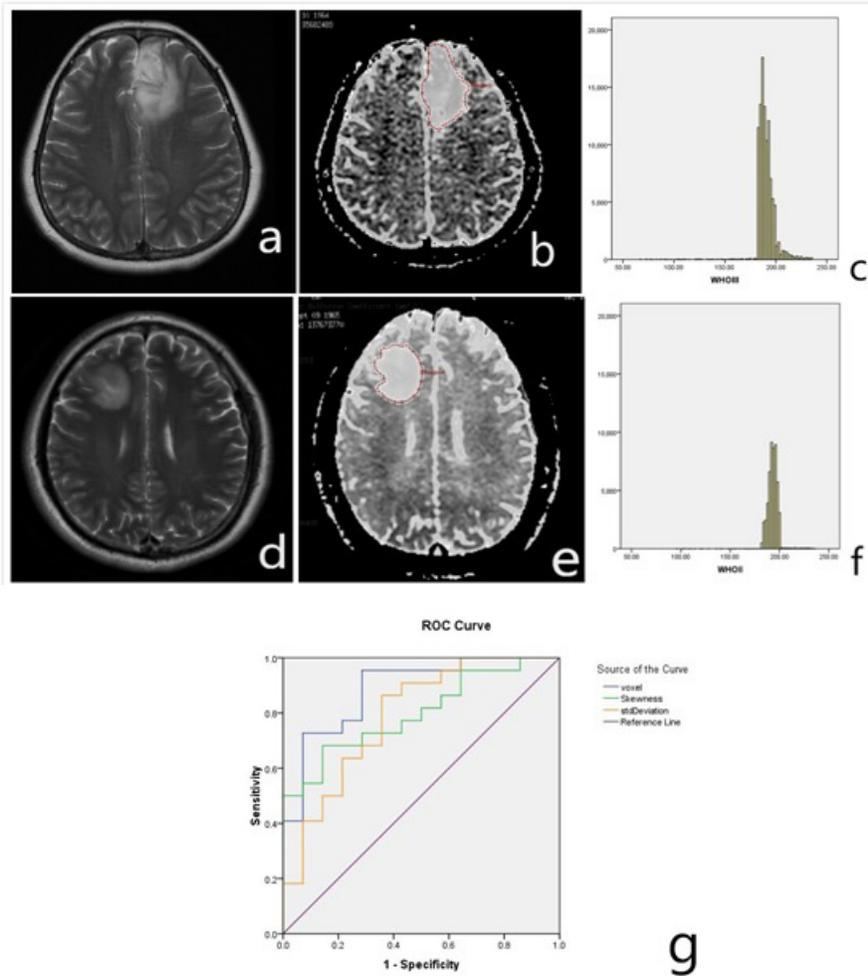
## 2. Method

Fourteen patients with grade II glioma and 22 patients with grade III glioma were enrolled in this retrospective study, tumor grades were pathologically confirmed. All the participants underwent DWI on GE Signa HDxt 3.0T MR whole body scanner. ROIs that contained the entire tumor and peripheral edema were drawn in each slice of the ADC maps. Then histograms voxel wise measurements of the entire tumor volume were obtained. Histogram related parameters including min intensity, max intensity, mean value,

median intensity, the 10th,25th,50th,75th and 90th percentiles, range, voxel number, std deviation, variance, relative deviation, mean deviation, skewness, kurtosis and uniformity were recorded. The obtained parameters were compared between groups through the SPSS 18.0. Receiver operating characteristic curve (ROC) was used to assess the ability of parameters between grade II and III glioma. All statistical results were  $P < 0.05$  as statistically significant.

## 3. Results

The ADC map and histogram of typical cases grade II and III glioma are shown in Figure 1. The histogram parameters of grade II and III and comparison results are summarized in Table 1. It can be seen that min intensity, max intensity, mean value, median intensity, the 10th, 25th, 50th, 75th and 90th percentiles, skewness, kurtosis and uniformity are decreased in grade III than grade II, and on the contrary range, voxel number, std deviation, variance, relative deviation, mean deviation are increased. Among all, min intensity ( $p=0.045$ ), 10th percentiles ( $p=0.043$ ), voxel number ( $p=0.0041$ ), std deviation ( $p=0.013$ ), skewness ( $p=0.021$ ) showed significant difference between two groups. The ROC test showed that Min Intensity, 10th percentiles, Voxel number, std Deviation, Skewness feature significant difference between grade II and III (Figure 2), The AUC, cutoff value, sensitivity and specificity of the parameters are summarized in Table 2.



**Figure a:** grade III, T2WI shows mix-intensity, with edema. Figure d, grade II shows uniform slightly-higher-intensity on T2WI. In ADC maps (figure b&e) ROI was drawn including entire tumor and edema. The histogram curve center deviation turn to left in fig c, and right in fig f. ROC curve (figure. g) of voxel number, std deviation and skewness, the AUC is 0.899,0.789,0.799.

**Table 1: Histogram parameters of ADC signal values between grade II and III glioma**

ADC signal value Histogram analysis parameter	grade II (n=14)	grade III (n=22)	p value
Min intensity	$(1.22 \pm 0.42) \times 10^2$	$(1.03 \pm 0.59) \times 10^2$	0.045*
Max intensity	$(2.31 \pm 0.09) \times 10^2$	$(2.28 \pm 0.12) \times 10^2$	0.435
Median intensity	$(1.94 \pm 0.05) \times 10^2$	$(1.93 \pm 0.04) \times 10^2$	0.552
Mean value	$(1.93 \pm 0.06) \times 10^2$	$(1.93 \pm 0.05) \times 10^2$	0.745
10th percentiles	$(1.83 \pm 0.04) \times 10^2$	$(1.66 \pm 0.36) \times 10^2$	0.043*
25th percentiles	$(1.87 \pm 0.07) \times 10^2$	$(1.82 \pm 0.23) \times 10^2$	0.561
50th percentiles	$(1.94 \pm 0.05) \times 10^2$	$(1.94 \pm 0.06) \times 10^2$	0.662
75th percentiles	$(1.94 \pm 0.05) \times 10^2$	$(1.94 \pm 0.06) \times 10^2$	0.764
90th percentiles	$(2.01 \pm 0.09) \times 10^2$	$(2.00 \pm 0.09) \times 10^2$	0.746
range	$(1.11 \pm 0.47) \times 10^2$	$(1.25 \pm 0.60) \times 10^2$	0.443
Voxel number *	$(5.24 \pm 2.48) \times 10^6$	$(6.54 \pm 3.26) \times 10^6$	0.004*
Std deviation	$(1.3 \pm 0.1) \times 10$	$(1.6 \pm 1.4) \times 10$	0.013*
Variance *	$(1.18 \pm 0.27) \times 10^2$	$(1.41 \pm 0.34) \times 10^2$	0.53
Mean deviation	$(6.2 \pm 0.6) \times 10$	$(6.4 \pm 1.1) \times 10$	0.437
Relative deviation	$(1.10 \pm 0.88) \times 10^4$	$(1.61 \pm 1.47) \times 10^4$	0.275
Skewness *	- 0.954 ± -1.530	- 2.310 ± -3.996	0.012*
Kurtosis *	6.769 ± 3.563	8.581 ± 4.484	0.705
Uniformity	0.932 ± 0.060	0.914 ± 0.085	0.514

Note. —\* on behalf of the nonnormal diatribution, representation with median value ± interquartile.  
 \* represents statistically significant ( P<0.05 )

Table 2: ADC signal value Histogram parameters diagnostic ability between WHO grade II and III

ADC signal value Histogram parameters	AUC	cutoff value	sensitivity	specificity
Voxel number	0.886	$5.46 \times 10^6$	0.864	0.714
Skewness	0.799	-1.920	0.682	0.857
Std deviation	0.789	14.310	0.636	0.786
10th percentiles	0.571	170.233	0.727	0.643
Min intensity	0.502	114.0	0.591	0.786

#### 4. Discussion and Conclusion

In this study, the ROIs encompassed the tumor parenchyma and peripheral edema, without avoiding cystic, necrosis and hemorrhage area, which are characteristics of grade III glioma, as compared to grade II. In addition, the boundaries of the tumor lesions may not be clear since the surrounding areas may be vascularized. Both facts support that the ROI based analysis should include the entire tumor volume rather than subsections. In this study, min intensity and 10th percentiles showed significant difference between grade II and III, suggesting that ADC value in low zone is more meaningful. In other words, the lower range of ADC better reflects the progress of higher cellularity. The difference of voxel number between grade II and III reflects the faster growth rate and more invasion range of grade III. Standard deviation shows the level of data dispersion, higher standard deviation of ADC indicates larger regions of cystic, necrosis or haemorrhage. Skewness describes the symmetry of the curve distribution. Compared with grade II, the ADC value of grade III concentrate on low zone, the center of the histogram curve was shifted to left. Overall, it is seen that histogram analysis of ADC signal value based on entire tumor could provide more information in differentiation of grade II and III glioma. Several parameter showed superior diagnostic value.

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