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Original Research Article

Diffusion Weighted Imaging and Grading of Brain Tumours

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ABSTRACT

Background: Most prevalent primary cerebral tumours are meningiomas. The other frequent intracranial tumours are pituitary adenomas, which are benign, and gliomas, which are intra-axial brain tumours. The objective of this study is to understand the importance of DW MRI imaging with standard b-value in differentiating presurgical grading of the brain tumour.

Design: A total of 24 DWI patients, including 12 meningiomas, 8 gliomas, and 4 pituitary adenomas, were included in this retrospective analysis.

Method: The Stejskal-Tanner equation is used to analyse the ADC_{mean}, ADC_{min}, and ADC_{max} values from the healthy and tumour core that are obtained out from area of interest (ROI).

Result: The ADC_{mean} value of Gliomas ranges from 0.09 x 10^{-3} mm^2s^{-1} to 0.99 x 10^{-3} mm^2s^{-1} with a median value of 0.25 x 10^{-3} mm^2s^{-1}. ADC_{mean} value 1.82 x 10^{-3} mm^2/s (sensitivity: 67%. Specificity: 81.8%) and 0.94 x 10^{-3} mm^2/s (sensitivity: 75%. specificity: 81.3%) can discriminate grade II –IV meningioma from grade II-IV glioma.

Conclusion: The ADC and its threshold levels offer crucial details on the grades, consistency, and characterization of tumour, aiding accurate diagnosis and therapy.

KEYWORDS: Brain tumour, Imaging, MRI, DWI, ADC, b-value.

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INTRODUCTION

The meningiomas are the most common primary intracranial tumours and represents 36% of central nervous system (CNS) tumour [1]. The gliomas are intra-axial brain tumour located frequently in the supratentorial region and accounts for 3.4% of all intracranial tumours [2]. The pituitary adenomas are mainly benign slow growing tumour arising from the pituitary gland. They are intensifying accompanies with disorder of hormones [3].

These tumours are frequently identified by histopathological examination. However, an improper selection of area for biopsy sample from brain tumours leads to error in microscopic diagnosis. Magnetic resonance imaging (MRI) is the noninvasive procedure suitable in resolving, management and forecasting prognosis of brain tumours. The Diffusion weighted imaging (DWI) is a

technique in magnetic resonance imaging which has bought distinctive change in imaging. It catches small motions of water molecules augmenting expression of intrinsic directionality in the brain [4]. Our body spaces contain water which provides a considerable element in body weight.

The diffusion of water molecules in tissues follows a definite pattern that captures the physiology by and reflects the difference in rate of diffusion in between tissues. The DWI is advised to trace the distinction between a benign and malignant brain tumour. Diffusion imaging predicated on ADC has indeed been tested for tumour assessment throughout the past two decades [5,6]. It has been proposed that analyzing the ADC of the lesion data could be of predictive as well as diagnostic significance [7,8]. Furthermore, preoperative diffusion values appear to be useful for differentiating radiation-induced brain injury from advanced disease and prognostic of clinical response to radiotherapy [8-11]. The Apparent diffusion coefficient (ADC) is the quantification of proportions of water molecules in the tissue analysed with DWI. The malignant tumour exhibit lower ADC value compared to benign tumours [12].

The values of ADC lower than 1×10^{-3} mm^2s^{-1} considered to be a malignant tumour [13]. However, some benign tumours demonstrate low ADC values and identified as malignant tumour. The value of ADC is considerably inversely proportional to cellularity of the brain tumour [14]. An improper selection of area for biopsy sample leads to error in microscopic diagnosis. The ADC values are utilized as a guide to forecast the outcome of the treatment in malignant tumours. It is necessary to identify the grade of the brain tumour and its expression possibilities with the aid of diffusion weighted imaging (DWI). The objective of this study is to analyze the apparent diffusion coefficient (ADC) value in distinguishing three common tumours that includes Meningioma, Gliomas and Pituitary adenomas.

Aim: The aim of this study is to understand the importance of DW MRI imaging with standard b-value in differentiating presurgical grading of the brain tumour.

METHOD

Study Design: It is a retrospective investigation of ADC values of three tumours. The cases of meningioma and glioblastoma were identified to persuade the research. A patient age limit of 5 years to 70 years was chosen comprising both genders and different races of Malaysia. A total of 33 patients (n=33) were selected for the study. These patients were diagnosed with brain tumour. Out of these 33 patients, 12 (n=12) meningiomas, 8 (n=8) glioma and 4 (n=4) pituitary adenoma patients underwent DWI. Patients with head injury, demyelinating diseases and meningitis were excluded from the study. The patient's data was collected from their case file (ARCHIVE) from Department of Neuroscience and the images of DWI were recovered from a public University hospital in Malaysia's picture archiving and communication system (PACS).

DWI images: The MRI of the patients were performed in Radiology in a public university hospital in Malaysia with Philips ACHEVA 3.0 Tesla MRI machine. A spin echo pulse sequence of [TR/TE] of 3433/93.8, flip angle 90° and 5mm slice thickness was stipulated in an axial plane. In DWI, magnitude of diffusion gradient (b value) of b = 0 s/mm^2 and b-value of 1000 s/mm^2 is applied in X, Y and Z axis maintaining a space of 6ms separating two slices.

Image Evaluation: A skilled radiologist and a well-trained radiographer retrospectively evaluated the DWI images A region of interest ROI were placed in the tumour core and another ROI was placed on the contralateral healthy area of the cerebral hemisphere to determine the apparent diffusion coefficient (ADC) which is estimated with Stejskal-Tanner equation (15). $ADC = -(1/b)\ln(S/S_0)$ where S_0 is intensity of the signal with gradient factor b=0; S is intensity of the signal with gradient factor b=1000 mm^2/s; 1n is natural algorithm and b in 1/*b* is 1000; The Values of ADC were expressed were illustrated with 10^{-3} mm^2/s

Statistical evaluation: The analysis of the data was carried out with SPSS version 23. The accumulated information of ADC values was estimated by descriptive analysis. Box plot and

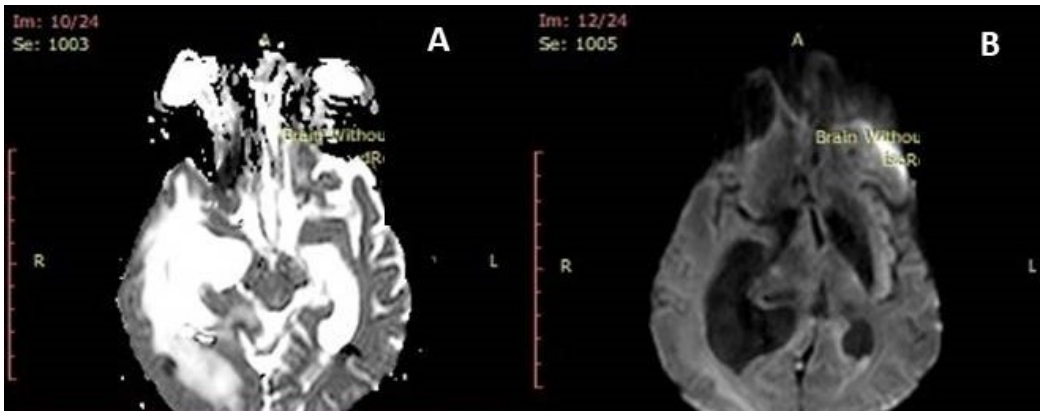

Fig. 1: A 56-year-old female with features of Grade I meningioma A) DWI at b_0 showing a hyperintense mass in the left anterior parasagittal region B) DWI at b_{1000} showing hypointense mass in left frontal region.

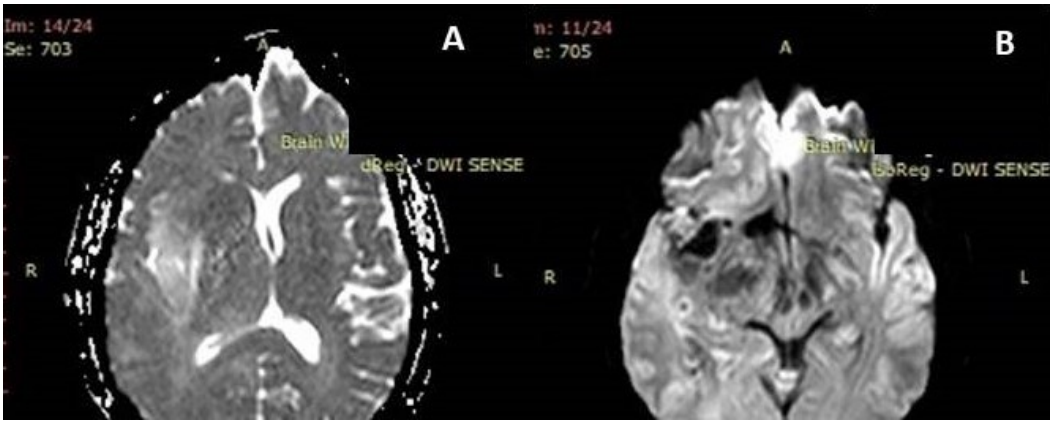

Fig. 2: A 48-year-old male with features of Grade I Glioma A) DWI at b_0 showing a isointense to hyperintense mass in the right posterior parietal lobe B) DWI at b_{1000} showing hypointense mass in right posterior parietal lobe.

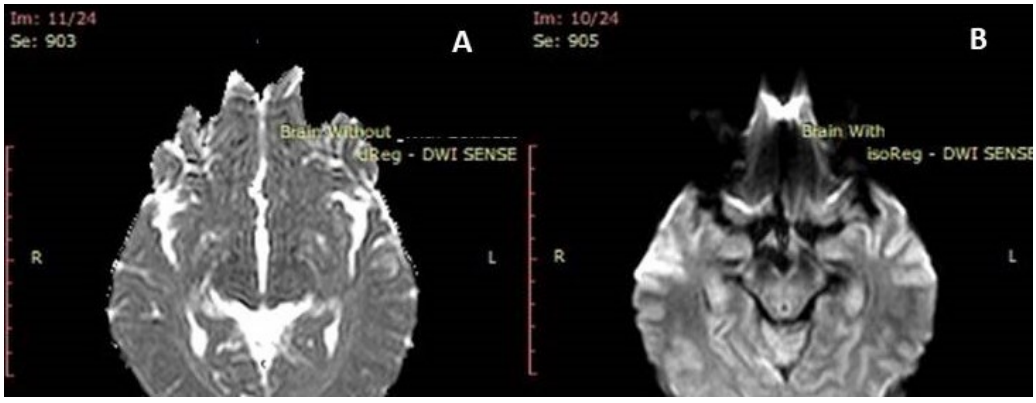

Fig. 3: A 46-year-old female with features of Grade I pituitary adenoma A) DWI at b_0 showing a hyperintense mass in the suprasellar region B) DWI at b_{1000} showing hypointense mass in the suprasellar region.

ROC curve analysis was performed to compare the tumour core ADC values of meningioma, glioma, and pituitary adenoma. The 2-tailed t test values of ADC of Meningiomas, Gliomas and Pituitary adenomas. The recorded variability was considered statistically significant if $P<0.05$. Normalized ADC (NADC) was calculated in every case as a ratio ADC_{mean} meningioma/ ADC_{mean} white matter.

RESULTS

Meningioma: The ADC_{mean} value of meningioma ranges from 0.15 x 10^{-3} mm^2s^{-1} to 2.55 x 10^{-3} mm^2s^{-1}. Meningioma grade I has an ADCmean value of 0.79 ± 0.76 x 10^{-3} mm^2s^{-} , while meningioma grades II to IV have an ADC_{mean} value of 0.16 ± 0.50 x 10^{-3} mm^2s^{-1}. In high grade compared to grade I meningioma, the ADC_{mean} is lower. Meningioma grade I has an ADC_{min} value of 0.72 ± 0.86 x 10^{-3} mm^2s^{-1} , and meningioma grades II through IV have an ADC_{min} value of 0.15 ± 0.07 x 10^{-3} mm^2s^{-1}. Meningioma grade I has an ADC_{max} value of 0.61 ± 0.67 x 10^{-3} mm^2s^{-1} , and meningioma grades II through IV have an ADCmax value of 0.17 ± 0.10 x 10^{-3} mm^2s^{-1}. Meningioma grade I has a

Table 1: ADC_{mean}, ADC_{min}, ADC_{max}, and NADC values in three different brain tumours.

	Meningioma		Glioma		Pituitary adenoma
	Grade I	Grade II-IV	Grade I	Grade II-IV	Grade I
ADCmean	0.79 ± 0.76	0.16 ± 0.50	0.40 ± 0.32	0.20 ± 0.14	0.74 ± 0.33
ADCmin	0.72 ± 0.86	0.15 ± 0.07	0.50 ± 0.56	0.13 ± 0.12	0.82 ± 1.53
ADCmax	0.61 ± 0.67	0.17 ± 0.10	0.33 ± 0.18	0.28 ± 0.24	0.51 ± 0.84
NADC	0.60 ± 0.47	0.07 ± 0.03	0.19 ± 0.15	0.14 ± 0.05	0.57 ± 1.03

Table 2: The mean ADC values of different grade of brain tumours using standard b-values by diffusion weighted imaging.

	Area under curve(AUC)(95%CI)	P value	Cut off ADC value	Senstivity (%)(95%CI)	Specificity (%)(95%CI)	Younde-n Index
ADC_{mean} Meningioma G1	0.8(65.2-97.8)	0.02	0.88x10-3	72.0 (64.0 -100.0)	81.4(64.3-8.7)	0.54
ADC_{mean} Meningioma G2, G4	0.73 (56.0-82.1)	0.25	1.82x10-3	67.0 (50.0-100.0)	81.8(54.5-90.9)	0.56
ADC_{min} Meningioma G1	0.71 (52.1-87.2)	0.29	0.85x10-3	80.0(60.0-90.0)	78.6(57.1-85.7)	0.64
ADC_{min} Meningioma G2,G4	0.69.5(51.0-72.5)	0.52	0.74x10-3	75.1(57.3-86.1)	86.4(63.3-95.5)	0.62
ADC_{max} Meningioma G1	0.93(73.5-95.3)	0.34	0.90x10-3	78.3(56.9-90.0)	72.4(57.1-85.7)	0.67
ADC_{max} Meningioma G2, G4	73.5(53.0-85.0)	0.45	0.85x10-3	70.0(55.4-84.8)	86.4(59.1-100.0)	0.66
ADC_{mean} Glioma G1,G4	0.82(72.0-94.0)	0.62	0.94x10-3	75.0(64.3-85.5)	81.3(56.3-100.0)	0.68
ADC_{min} Glioma G1,G4	0.80(65.1-90.0)	0.36	0.87x10-3	76.0(62.5-87.5)	75.0(62.8-100.0)	0.63
ADC_{max} Glioma G1,G4	0.85(68.0-92.8)	0.54	0.90x10-3	87.5(52.3-1.00)	87.5(55.4-100.0)	0.62

NADC value of 0.60 ± 0.47 x 10^{-3} mm^2s^{-1} , and meningioma grades II through IV have a value of 0.07 ± 0.03 x 10^{-3} mm^2s^{-1}.

Gliomas

The ADC_{mean} value of Gliomas ranges from 0.09 x 10^{-3} mm^2s^{-1} to 0.99 x 10^{-3} mm^2s^{-1} with a median value of 0.25 x 10^{-3} mm^2s^{-1}. The ADC_{mean} value for grades I-IV glioma is 0.40 ± 0.32 x 10^{-3} mm^2s^{-1} and 0.20 ± 0.14 x 10^{-3} mm^2s^{-1} respectively. In high grade compared to grade I glioma, the ADC_{mean} is lower. The ADC_{min} value for gliomas in grades I through IV is 0.50 ± 0.56 x 10^{-3} mm^2s^{-1} and 0.13 ± 0.12 x 10^{-3} mm^2s^{-1} respectively. The ADC_{max} value for gliomas in grades I through IV is 0.33 ± 0.18 x 10^{-3} mm^2s^{-1} and 0.28 ± 0.24 x 10^{-3} mm^2s^{-1} respectively. Meningioma grade I has a NADC value of 0.19 ± 0.15 x 10^{-3} mm^2s^{-1}, and meningioma grades II through IV have a value of 0.14 ± 0.05 x 10^{-3} mm^2s^{-1}.

Pituitary adenoma: The ADC_{mean} value of Pituitary adenoma ranges from 0.60 x 10^{-3} mm^2s^{-1} to 2.77 x 10^{-3} mm^2s^{-1} with a median value of 0.19 x 10^{-3} mm^2s^{-1}. Grade I pituitary adenomas are recognized. The value of its ADC_{mean} is 0.74 ± 0.33 x 10^{-3} mm^2s^{-1}. The tumours ADCmin mean value is 0.82 ± 1.53 x 10^{-3} mm^2s^{-1}. These tumours ADCmax value is calculated to be 0.51 ± 0.84 x 10^{-3} mm^2s^{-1}. The tumor's NADC value is 0.57 ± 1.03 x 10^{-3} mm^2s^{-1}.

According to Table I, the ADC_{mean}, ADC_{min}, ADC_{max}, and NADC values were higher in Grade I meningioma compared to Grade I pituitary adenomas. Grade II-IV meningiomas have lower values than Grade II-IV gliomas.

Only ADC_{mean} for Grade I meningioma from the ROC curve analysis were statistically significant, despite the fact that there were some statistically significant disparities across the grades.

DISCUSSION

DWI is crucial for imaging brain tumour, particularly for finding their grade. This MRI modality is also essential to determine the outcome of the management of these tumours. There are few investigations on meningiomas, gliomas and pituitary adenomas on quality of their diffusion and differentiation between their grades in accordance with DWI and ADC values [16]. ADC offers critical extra information beyond what MRI can. This study has

demonstrated that there are differences in ADC grades between meningioma, glioblastoma, and pituitary adenoma, but not enough to differentiate between the different primary cancer types [17,18].

This could be because of the ADC expressing more universal traits like cellular proliferation. ADC levels often are less in primary brain tumours with more cellular proliferation in contrast to normal brain parenchyma [19,20].

In present study the ADC_{mean} of grade I meningioma is slightly higher than glioblastoma. In a study in 39 meningioma patients, the ADC_{mean} was higher in lower grade compared to the higher grade. However, when compared to benign lesions, atypical and malignant meningiomas exhibits lower ADC values [21,22]. ADC_{mean} is less relevant to tumour cellularity than ADC_{min} [23]. ADC_{mean} value may be used to identify cancers with a high differentiation activity using the specified threshold. Many explanations, including greater tumour cellularity, tumour pattern, fibrous or gliotic tissues, or a combination of these characteristics, have been put up to explain the lower ADC in high-grade tumours [24]. Analyses of ADC values would make a big difference in the identification and differential diagnosis. Main benefit include not requiring contrast material and quick and easy imaging capture within seconds [25]. When employing a typical b-value DW-MRI, a minimum ADC threshold of 1.070 X 10^{-3} mm^2/s gave 79.7% sensitivity and 60.0% specificity is pertinent for identifying high-grade gliomas(26). The results of this study indicated an ADC_{min} threshold of 0.74 x 10^{-3} mm^2/s (sensitivity: 75%. Specificity: 86.4%) and 0.87 x 10^{-3} mm^2/s (sensitivity:76%. specificity:75%) to discriminate grade II –IV meningioma from grade II-IV glioma. Additionally, ADC_{mean} value 1.82 x 10^{-3} mm^2/s (sensitivity: 67%. Specificity: 81.8%) and 0.94 x 10^{-3} mm^2/s (sensitivity:75%. specificity:81.3%) to discriminate grade II –IV meningioma from grade II-IV glioma. A similar study with standard b-value ADC images and a histogram estimation of the whole tumour volume was conducted to distinguish different glioma grading. According to their findings, grades II, III, and IV gliomas had distinct ADCmin values for standard b-value scans. They also found significant difference of ADC_{mean} for standard b-value between Grade II-IV tumour (27). The present study has shown a significant difference in ADC_{mean} that can discriminate Grade II-IV meningioma from grade II-IV glioma. The minimal level ADC value from b = 1000 DW-MRI inside that solid tumour region was substantially lower in high-grade (III and IV) gliomas than low-grade (II) gliomas at 3T, and a cutoff value of 0.90 X 10^{-3} mm^2/s was recommended to distinguish high and low-grade gliomas with 85% specificity and 71% specificity. The ADC_{max} is also higher in Grade I meningioma than Grade I pituitary adenoma. The ADC_{min} has been thoroughly investigated for glioma grading with 1.5T, high-grade (III and IV) and low-grade (I and II) tumours could be distinguished with 95% sensitivity and 80.6% specificity using a threshold of 1.48 for the lowest ADC within the tumour adjusted with the contralateral side collected using a standard b-value [28].

Strong tissue mechanisms and substantial water flow across capillaries hinder the tumor's definition. The ADC values are impacted by myelin, which has a stronger effect on the diffusing pattern. Despite the fact that various factors influence ADC values in brain tissues [29]. As an indicator for tumour cellularity, DWI is useful to discriminate between benign and malignant tumours by evaluating the ADC. It is also used to investigate heterogeneity [30].

The box plot Figure (A) depicts that NADC decreased from 0.25 units in Meningioma grade I to about 0.10 units. There is no significant increase for Glioma grade I – grade IV but potential increase is observed for Pituitary adenoma grade1 which ranged more than 2.0 units. There also appears to be major decrease in median NADC for Pituitary adenoma grade1compared to Meningioma grade I- grade IV, and Glioma grade I – grade IV which maintained consistent spread out. However, there is one outlier with high NADC in Glioma grade I – grade IV. This demonstrates that NADC values are significantly varies between Meningiomas, Gliomas and pituitary adenomas. In Figure (B) the boxplot exhibits

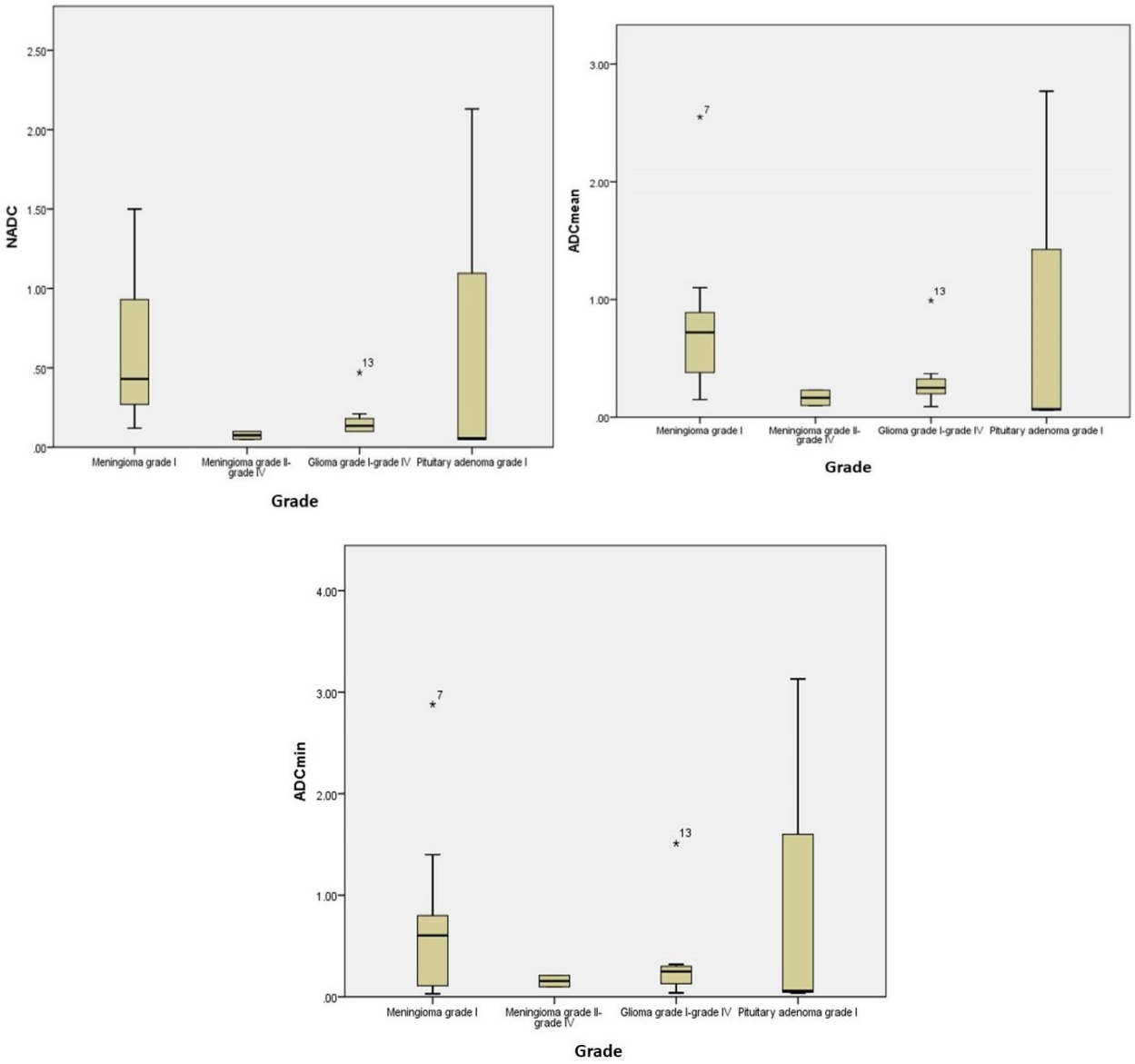

Fig. 4: Boxplots of ADC values of different grades of (A) Meningioma (B) Glioma (C) pituitary adenoma.

that ADC_{mean} for Meningioma grade I – grade IV and Glioma grade I- grade IV having same median unit. Consequently, Pituitary adenoma grade I showing low median unit. There is one high ADC_{mean} for Glioma grade I-Grade IV whereas there are no extreme indicators for the rest of the tumours. In Figure (C) Similarly, for ADC_{min}, Pituitary adenoma grade I has significant rise of patients compared to Meningioma and Glioma. There are high outliers for both Meningioma grade I and Glioma grade I- grade IV while the same spread for Meningioma grade I – grade IV and Glioma grade I – grade IV is noticed. Pituitary adenoma grade I specify uneven distribution with median lying at the bottom of the box.

This study has few limitations. The patient group is wide and there are only a limited number of patients. The use of ROI analysis to examine the performance of ADC derived parameters in tumor tissue areas for tumor grading was another limitation. Other limitation is that it is a retrospective study. The study only included one centre and had a smaller batch size of brain tumours. It is advised to do more research using a larger tumour collection and a multicenter strategy.

CONCLUSION

The study revealed numerous correlations between various DWI data. The Grade I meningioma had statistically significant higher ADC_{mean} than Grade I glioma. Overall, the findings of the present investigation point to the possibility that the ADC parameters obtained from conventional b-value DWI MRI

can be used to predict the grade of a tumour. The effectiveness of b-value of DW-MRI in the pre-operative screening of brain tumours needs to be confirmed in future investigations that should include more comparable patient populations.

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Author Contributions

The authors affirm that everyone listed is eligible to be an author and have checked the article for plagiarism. If plagiarism is found, all authors will be held accountable on an equal basis. The study was created and prepared by **MC, MFR and KG,** who also carried out the research, supplied the research tools, and gathered and organised the data. Data were examined and interpreted by **MC.** The article's first and last draughts were written by **MC,** who also helped with the logistics. The content and similarity score of the paper are the responsibility of all authors, who also gave the final text a critical assessment and approval.

Conflicts of Interests: None

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