ORIGINAL ARTICLE

# Diagnostic Accuracy of Apparent Diffusion Coefficient Value in Differentiating Benign and Malignant Brain Lesions Keeping Histopathology as Gold Standard

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**ABSTRACT**

**Objective:** The purpose of this study was to assess the competence of preoperative Apparent Diffusion Coefficient (ADC) values in predicting brain tumors as benign or malignant, keeping histopathology as the gold standard.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** The study was carried out at the Department of Diagnostic Radiology, POF Hospital, Wah Cantt, Pakistan, from December 12th 2020 to June 9th 2021.

**Materials and Methods:** The apparent diffusion coefficient (ADC) sequence is based on the diffusion properties of water molecules within tissues and correlates with tissue cellularity. ADC may have a role in predicting tumor grade for gliomas and may in turn, assist in identifying tumor biopsy sites.

A total of 140 patients were enrolled in the study. In all the images, the slice thickness was taken as 3mm, and the slice gap of 10. The mean age of the patients was 46.5±14.0 years. Males were predominant. The mean BMI was 26.8±5.5 kg/m2, and the mean duration of symptoms was 2.0±1.4 months.

**Results:** The mean age of the patients enrolled in the study was 46.5±14.0 years. Males were predominant; there were 85 males (60.7%) and 55 females (39.3%). The mean duration of symptoms was 2.0±1.4 months. A history of chronic headache was found in 100 patients (71.4%), a history of seizures in 20 (14.3%), and a history of focal deficit was present in 111 patients (79.3%). Apparent diffusion coefficient (ADC) value in differentiating benign and malignant brain lesions showed sensitivity 77.5%, specificity 91.6%, PPV 92.5%, NPV 75.3% and diagnostic accuracy 83.5%.

**Conclusion:** Overall, malignant brain lesions display lower ADC values than benign ones. Apparent diffusion coefficient (ADC) values improved our abilities to differentiate benign from malignant brain lesions.

**Keywords:** *Apparent Diffusion Coefficient, Brain Tumors, Histopathology.*

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## Introduction

With the rapidly increasing population, cancer has become a major global public health issue. Imaging plays a very decisive role in the analysis and diagnosis of patients having brain tumors.[1] With the increasing use of imaging, there has been an increase in the number of incidentally found brain lesions resulting in a treatment dilemma for physicians and emotional strain for patients and families.[2] One study found that out of 66 brain lesions, histopathology revealed 59% malignant and 41% benign lesions.[3] Though some radiological features on conventional neuroimaging like intratumoral cystic changes, hyperostosis of the adjacent skull, bony destruction, extracranial tumor extension through the skull base, arterial encasement, and peritumoral brain edema have been found to distinguish these two entities; no single feature has been found to be highly reliable.[4,5]

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Diffusion-weighted MRI (DWI) might be of value in tumor assessment, as it has the ability to provide tissue contrast based on molecular diffusion. Initially, DWI in other than intracranial sites did not yield sufficient image quality due to susceptibility artifacts and motion artifacts. More recently, technical advances in MRI, like the development of parallel imaging, high gradient amplitudes, and multichannel coils, have enabled the performance of DWI. The net diffusion of the water molecules is referred to as the apparent diffusion coefficient (ADC). The high sensitivity and specificity of DWI in the diagnosis of acute cerebral infarction are widely accepted.[6,7] Combining diffusion-weighted imaging with conventional MRI sequences can give a sensitivity of up to 100% in differentiating benign and malignant lesions, thereby eliminating the need for biopsy and histopathology.[8] ADC values play a limited role in distinguishing between malignant and benign lesions in the head and neck region. It may be only suggested that lesions with mean ADC values above 1.75x10 -3 mm2/s are probably benign. Further large studies are needed for the analysis of the role of diffusion-weighted imaging/ADC in the discrimination of benign and malignant lesions in the head and neck region.[9]

The validity of ADC in predicting a malignant or benign diffuse orbital mass had a sensitivity of 87%, specificity of 67%, and accuracy of 88%.[10] Another study reported that diffusion-weighted imaging by using ADC value showed a sensitivity of 97.6% and specificity of 98.7% in detecting malignant hepatic lesions from benign ones ($p$=0.0001, AUC = 0.99).[11] One study found ADC thresholds of 1.23x10 -3 mm2/s (sensitivity, 75. %; specificity, 92.3%, accuracy, 84.6%).[12]

The rationale of this study is to assess the diagnostic accuracy of ADC value in differentiating benign and malignant brain lesions keeping histopathology as the gold standard. Through literature, it has been noticed that ADC can be helpful and accurate enough that it can replace interventional procedures including biopsy or histopathology. But varied data has been retrieved regarding the accuracy of ADC for the detection of brain tumors as benign or malignant. Moreover, there are no local studies found in the literature. In many settings, especially in peripheral areas, the facility of neurosurgeon and facility operation theatres is not available, and this also increases the referral and burden on settings where neurosurgeon and appropriate equipment is available. So, to confirm the evidence, we want to conduct this study so that the results of this study can be implemented in a local setting, and we can recommend the diagnosis of the type of brain tumor instead of going for interventional procedures, especially for benign lesions.

## Materials and Methods

This was a cross-sectional validation study done in the Department of Radiology, POF Hospital, Wah Cantt, Pakistan over a period of six months from December 10th, 2020, to June 9th 2021. A sample size of 140 cases was calculated with a 95% confidence level, an expected percentage of malignant brain tumors i.e., 59%[3], and sensitivity of ADC i.e., 75%[12] with a 9.5% margin of error and specificity of ADC 92.3% with 7% margin of error.

Sampling: Non-probability consecutive sampling.

Patients aged 20-70 years of either gender, 75 presenting with brain lesions (detected on CT brain), planned to undergo histopathology under general anaesthesia.

Patients with recurrent tumor, incomplete resection of the previous tumor, epidermoid tumor, cystic tumor, metastatic disease (on medical record).

**Data Collection Procedure**

One hundred forty cases fulfilling inclusion criteria were enrolled in the study and referred to the Department of Radiology, POF Hospital, Wah Cantt. Informed consent was taken. Demographic data (including name, age, gender, duration of symptoms, h/o chronic headache, seizure, and focal deficit) were noted. Then patients underwent MRI using 1.5-T MR systems (Siemens Medical Solutions, Erlangen, Germany) by a researcher under the supervision of a consultant radiologist having four years of experience in MRI use. The scanning protocols include the following sequence and images, i.e., turbo spin echo (tse), T2 weighted images (3920/102), T2 FLAIR (fluid-attenuated inversion recovery sequence), (9000/111), 76 turbo spine echo, TI weighted images (488/10), diffusion-weighted images (8500/110), and GRE (gradients recall echo) sequence. All these images were taken in the axial plane. In addition, the coronal and sagittal plane images of T2 weighted sequences were also

taken, and ADC mapping was done within the diffusion-weighted image by the calculation done through software. In all the images slice thickness was taken as 3mm and the slice gap of 10%. For the good resolution of the image, 256x256 matric size was taken. Patients were labelled as positive or negative (as per operational definition). Then all patients underwent histopathology by a single surgical team and a biopsy sample was sent to the laboratory of the hospital for confirmation of brain tumor either benign or malignant (as per operational definition). All the information was collected on a pre-designed proforma (attached).

**Data Analysis Procedure**

All the collected data were entered and analyzed through SPSS version 20. Quantitative data like age, BMI, duration of symptoms, and ADC were presented as mean + SD. Qualitative data like gender, h/o chronic headache, seizure, and focal deficit were presented as frequency and percentage. A 2x2 table was generated to calculate the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of ADC taking histopathology as the gold standard. Data were stratified for age, gender, BMI, duration of symptoms, h/o chronic headache, seizure, and focal deficit. Post-stratification, 2x2 tables were generated to calculate sensitivity and specificity. PPV, NPV, and diagnostic accuracy of ADC taking histopathology as the gold standard.

## Results

The mean age of the patients enrolled in the study was 46.5±14.0 years. Males were predominant; there were 85 males (60.7%) and 55 females (39.3%). The mean duration of symptoms was 2.0±1.4 months. A history of chronic headache was found in 100 patients (71.4%), a history of seizures in 20 (14.3%), and a history of focal deficit was present in 111 patients (79.3%). Apparent diffusion coefficient (ADC) value in differentiating benign and malignant brain lesions showed sensitivity 77.5%, specificity 91.6%, PPV 92.5%, NPV 75.3% and diagnostic accuracy 83.5%. (Table 1).

**Table 1: Diagnostic accuracy of apparent diffusion coefficient (ADC) value in differentiating benign and malignant brain lesions keeping histopathology as the gold standard (n = 140)**

| | Histopathology (Gold Standard) | | |
|---|---|---|---|
| **ADC** | **Malignant** | **Benign** | **Total** |
| Malignant | 62 (TP) A | 5 (FP) B | 67 |
| Benign | 18 (FN) C | 55 (TN) D | 73 |
| Total | 80 a+c | 60 b+d | 140 |

| | | |
|---|---|---|
| Sensitivity: a/a+c | x 100 | 77.5% |
| Specificity: d/d+b | x 100 | 91.6% |
| Positive Predictive Value: a/a+b | x 100 | 92.5% |
| Negative Predictive Value: d/c+d | x 100 | 75.3% |
| Diagnostic accuracy: a+d/a+d+b+c | x 100 | 83.5% |

## Discussion

Over the past two decades, magnetic resonance (MR) imaging (MRI) has proven to be a valuable diagnostic tool in oncology.[13] Rapid improvements in MRI techniques have resulted in MR images with excellent spatial resolution and soft tissue contrast, which contribute to the differentiation of suspected tumors. However, using conventional MRI sequences, difficulty in differentiating benign from malignant lesions may arise when malignant and benign lesions share certain morphologic and contrast-enhancement characteristics. In these cases, diffusion-weighted MR imaging (DWI) might be of value in tumor assessment, as it has the ability to provide tissue contrast based on molecular diffusion.[14]

Diffusion-weighted images can be assessed in two ways; qualitatively by visual assessment of the signal intensity and quantitatively by measurement of the apparent diffusion coefficient (ADC). The ADC value quantifies water proton motion, which in biological tissues is a combination of true water diffusion and capillary perfusion.

Malignant tumors are reported to have a high cellular density and low extracellular space volume, which is associated with impeded water proton diffusion and low ADC values. In contrast, various benign lesions are characterized by an increased amount of extracellular matrix with minimal increase in cellular density, which may result in higher ADCs.[15,16]

The presence of indeterminate brain lesions on imaging can pose a clinical dilemma that sometimes entails consideration of the costs and risks associated with biopsy. DWI is potentially useful for guiding such clinical decisions. Indeed, the results for calvaria and skull base lesions in this report and for brain base lesions in prior studies indicate that ADC values in malignant brain lesions are, in general, significantly lower than ADC values in benign lesions.[17,18]

Brain neoplasms are a heterogeneous group, both in

histopathological types and the primary location. The variety of brain tumors cause great difficulties in the diagnosis; it requires specialized and specific multidisciplinary approaches.[19]

Neoplasms occurring in the CNS are derived from various primary germplasms and, consequently, from different tissues.[20] Histopathological examination is the basis of tumor diagnoses.[21]

Previous reports suggest an increasing value of MR diffusion imaging with the assessment of ADC in the diagnosis and differentiation of brain tumors.[22-25]

It is believed that the high cell density of primary malignant tumors is the cause of changes in tumor diffusion and reduction of ADC values. The ADC coefficient correlates with the total surface/volume of the nuclei and the degree of malignancy - the primary malignant tumors of the central nervous system are characterized by higher cell density and lowering of the ADC.[26]

Examples of one benign and one malignant tumor are shown in Figure 1 and Figure 2 respectively.

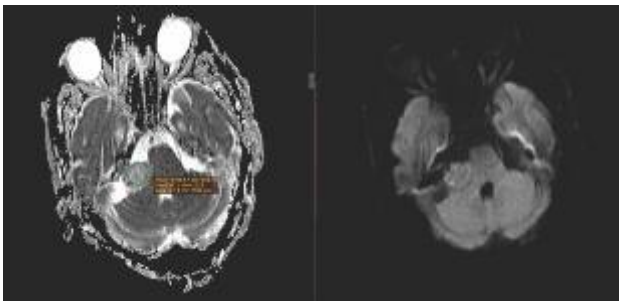

**Fig 1: An MRI (DWI & ADC) image of a benign CP angle tumor (Schawanoma). An ellipse ROI placed over the tumor gives a mean ADC value of 1.4 X $10^{-3}mm^2/s$**

Figure 1 shows a case of right CP angle Schwannoma, less commonly called neurinoma or neurilemmoma. It is a benign tumor of Schwann cell origin and the most common tumor of peripheral nerves, including cranial nerves. It often shows a higher signal on both DWI and ADC (T2 shine through - not restricted diffusion). Its ADC values are high falling in the benign category.

Figure 2 shows a case of biopsy-proven Glioblastoma with a mean ADC value of 1.0 X 10-3mm2/s. Glioblastomas are the most common adult primary brain tumor and are aggressive, relatively resistant to therapy, and have a corresponding poor prognosis.

In the current study, the diagnostic accuracy of apparent diffusion coefficient (ADC) value in differentiating benign and malignant brain lesions as follows: sensitivity 77.5%, specificity 91.6%, PPV 92.5%, NPV 75.3% and diagnostic accuracy 83.5%. Our results are comparable with Avendano et al. and Ginat et al.[3,12]

**Fig 2: An MRI (ADC, DWI & FLAIR) image of a biopsy-proven case of glioblastoma. An ellipse ROI placed over solid part of the tumor shows a mean ADC value of 1.0 X $10^{-3}mm^2/s$**

Another study by Sohu et al5 compared ADC value with histopathology to find out benign and malignant lesions, resulting in a sensitivity of 84.4%, specificity of 82.3%, PPV of 97.4%, NPV of 40%, and accuracy of 84.2%, these findings are in agreement with our results.

A study done by Surov A et al. supports our study findings, they determined the ADC sensitivity of 72.9%; specificity of 73.1%; accuracy of 73.0%; the positive predictive value of 33.3%, and negative predictive value of 96.8%, respectively taking histopathology as the gold standard to differentiate between benign and malignant lesions.[4]

Abdel-Salam and Mokhtar found the sensitivity, specificity, PPV, NPV, and accuracy of ADC in differentiating brain tumors from benign to malignant 89%, 100%, 100%, 86%, and 93% respectively. The results of their study are also consistent with the present study.[27]

## Conclusion

Overall, malignant brain lesions display lower ADC values than their benign counterparts. Apparent diffusion coefficient (ADC) values improved our ability to differentiate benign from malignant brain lesions.

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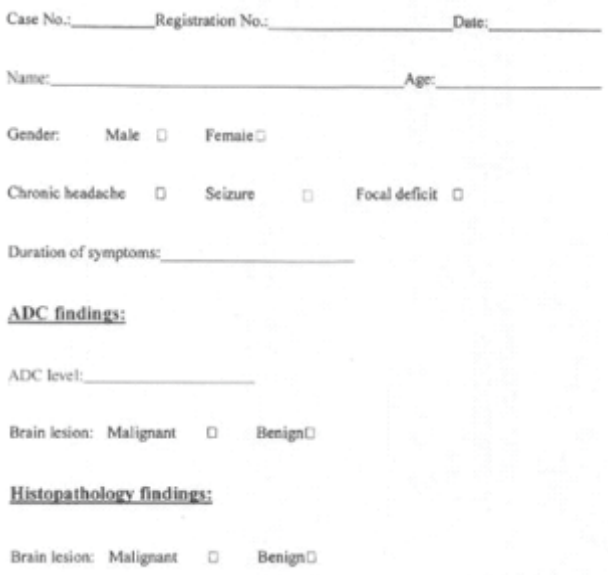
## Appendices

Diagnostic Accuracy of Apparent Diffusion Coefficient (ADC) Value in Differentiating Benign and Malignant Brain Lesions Keeping Histopathology as the Gold Standard.

## Proforma



Case No.:_____Registration No.:_____Date:_____

Name:_____Age:_____

Gender: Male ☐ Female☐

Chronic headache ☐ Seizure ☐ Focal deficit ☐

Duration of symptoms:_____

**ADC findings:**

ADC level:_____

Brain lesion: Malignant ☐ Benign☐

**Histopathology findings:**

Brain lesion: Malignant ☐ Benign☐

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