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## ORIGINAL ARTICLE

# Is Apparent Diffusion Coefficient Value Measured on Picture Archiving and Communication System Workstation Helpful in Prediction of High-grade Meningioma?

**S Hirunpat[1], N Sanghan[1], C Watcharakul[1], K Kayasut[2], N Ina[1], H Pornrujee[1]**

*Departments of [1]Radiology and [2]Pathology, Prince of Songkla University, Hat-Yai, Songkhla, Thailand*

## ABSTRACT

***Objective:*** *To determine whether the apparent diffusion coefficient (ADC) value measured on picture archiving and communication system (PACS) workstation is helpful in prediction of high-grade meningioma (World Health Organization grade II and III).*

***Methods:*** *A total of 28 patients (mean age, 58; range, 44-71 years) including 9 men and 19 women with histopathologically confirmed meningioma (20 benign, 7 atypical, and 1 malignant) between August 2010 and June 2014 were included in the study. All patients underwent preoperative standard brain imaging that routinely included diffusion-weighted imaging obtained at B value = 0 and 1000 s/mm$^2$. Quantitative analysis of the ADC value of the tumour and mean normalised ADC ratio of the tumour compared with the contralateral normal white matter were calculated and analysed.*

***Results:*** *The mean ADC value of atypical and malignant meningiomas (0.698 x 10$^{-3}$ mm$^2$/s ± 0.06 x 10$^{-3}$ mm$^2$/s) was significantly lower ($p < 0.05$) compared with that of benign meningiomas (0.83 x 10$^{-3}$ mm$^2$/s ± 0.37 x 10$^{-3}$ mm$^2$/s). The mean normalised ADC ratio in the atypical and malignant type (0.895 ± 0.09) was also lower than that in the benign type (1.05 ± 0.05) but was statistically insignificant ($p = 0.06$). Using a mean ADC value of less than 0.8 x 10$^{-3}$ mm$^2$/s as a predictor of high-grade meningioma gave a sensitivity of 75% (95% confidence interval, 34.9-96.8), specificity of 65% (40.8-84.6), positive predictive value of 46.2% (19.2-74.9), and negative predictive value of 86.7% (59.5-98.3).*

***Conclusions:*** *The mean ADC value of atypical and malignant meningiomas, measured conveniently by PACS, was statistically significantly lower than that of benign meningiomas and may be a helpful method in the prediction of high-grade meningioma with considerable sensitivity and specificity.*

***Key Words:*** *Brain neoplasms; Diffusion magnetic resonance imaging; Magnetic resonance imaging; Meningioma; Neoplasm grading*

***Correspondence:*** *Dr Siriporn Hirunpat, Department of Radiology, Prince of Songkla University, Hat-Yai, Songkhla, Thailand.*
*Email: hirsirip@hotmail.com*

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# 中文摘要

## 從PACS系統工作站量得的表觀擴散係數對於預測高度惡性腦膜瘤是否有幫助？

S Hirunpat, N Sanghan, C Watcharakul, K Kayasut, N Ina, H Pornrujee

**目的：**探討從影像存檔和通訊系統的工作站（PACS）量度得到的表觀擴散係數（ADC）對於預測高度惡性腦膜瘤（世界衛生組織II級和III級）是否有幫助。

**方法：**2010年8月至2014年6月期間經病理學證實為腦膜瘤的28名患者列入研究範圍，包括9男19女，平均年齡58歲（44-71歲）。患者中良性腦膜瘤20例、非典型腦膜瘤7例、惡性1例。所有患者接受標準的術前腦成像，一般包括B值=0和1000 s/mm²的彌散加權成像。然後計算腫瘤的ADC值和其與對側正常白質ADC的比值。

**結果：**非典型性和惡性腦膜瘤的平均ADC值（$0.698 \times 10^{-3}$ mm²/s ± $0.06 \times 10^{-3}$ mm²/s）比良性腦膜瘤的平均ADC值（$0.83 \times 10^{-3}$ mm²/s ± $0.37 \times 10^{-3}$ mm²/s）顯著為低（$p<0.05$）。腫瘤的ADC值和其與對側正常白質ADC的比值在非典型和惡性腦膜瘤（0.895 ± 0.09）也較良性腦膜瘤的低（1.05 ± 0.05），但未達統計學意義（$p=0.06$）。使用低於$0.8 \times 10^{-3}$ mm²/s的平均ADC值作為預測高度惡性腦膜瘤的敏感性為75%（95%置信區間34.9-96.8）、特異性65%（95%置信區間40.8-84.6）、陽性預測值46.2%（95%置信區間19.2-74.9）、陰性預測值86.7%（95%置信區間59.5-98.3）。

**結論：**從PACS量度出來的非典型和惡性腦膜瘤的平均ADC值比良性腦膜瘤明顯低，由於有一定的靈敏度和特異性，它可能是預測高度惡性腦膜瘤的一個有幫助的方法。

## INTRODUCTION

Meningioma is the most common benign intracranial tumour, accounting for 24% to 30% of all primary intracranial tumours.[1] Although meningiomas are generally considered benign and can be cured by surgical removal, up to 10% of these tumours are atypical or malignant (World Health Organization [WHO] grade II and III).[2] High-grade meningiomas (grade II and III) grow aggressively and recur frequently, resulting in higher mortality and morbidity than grade I. Early prediction of high-grade meningioma is therefore important, because it aids in preoperative surgical planning and determination of frequency of radiological examination in cases of observation without surgery.[3]

Typical meningioma is easily diagnosed, but the distinction between low-grade and high-grade meningioma using conventional magnetic resonance imaging (MRI) is difficult. Heterogeneous enhancement and irregular cerebral surface that may help differentiate the two groups[4] are still not consistent and unique neuroimaging features for diagnosing malignant meningiomas.[5]

Diffusion-weighted imaging (DWI) along with the calculation of apparent diffusion coefficient (ADC) have been reported to be a non-invasive and reliable technique in the distinction and differentiation of benign from malignant / atypical meningiomas on the basis of ADC maps and ADC value.[2,5-7] Most publications, however, calculated ADC value on a separate specialised workstation.[2,5-7] To the best of our knowledge, no publication has discussed calculation of ADC value in meningioma using a routine picture archiving and communication system (PACS) workstation. ADC value measured in liver nodules on a PACS workstation has already been reported to be as accurate as the value obtained on a dedicated specialised workstation and should also be applied to lesions elsewhere in the body.[8] For most radiologists, measurement of the ADC on a separate specialised workstation may be inconvenient and time-consuming.

The objective of our study was to determine whether ADC value measured on our PACS workstation in patients with meningioma could help predict high-grade meningioma.

## METHODS

This retrospective study was approved by our Institutional Review Board. The medical records and MRIs from the PACS (Synapse PACS, Fujifilm version 3.2.0) of 28 patients (mean age, 58; age range, 44-71 years) including 9 men and 19 women with histopathologically confirmed meningiomas (20 benign, 7 atypical, and 1 malignant) between August 2010 and June 2014 were included in the study. All patients underwent preoperative MRI studies on a 3 Tesla clinical scanner (Achieva; Philips Medical Imaging System, Best, The Netherlands), equipped with an 8-channel head coil and SENSE factor. Our standard brain protocol routinely included DWI obtained at B value of 0 and 1000 s/mm$^2$, via a single shot, spin-echo, echo-planar sequence. Trace images were obtained by simultaneous application of diffusion-sensitive gradients in three different directions (x, y, z gradients). Technical parameters were as follows: TR/TE 2400/75 ms, NEX 3, matrix 256×256, field of view 21×21 cm, slice thickness 5 mm, and slice gap 0-1.5 mm. ADC maps were automatically generated.

Two neuroradiologists who were blinded to the histological findings analysed the preoperative MR studies from our routine PACS workstation together. The DWI scans were visually inspected and classified as hyperintense, isointense, hypointense, or mixed signal intensity compared with normal white matter. The ADC value of each tumour was measured manually in the solid part of the tumour, avoiding the cystic, calcified, and haemorrhagic portions. The regions of interest (ROIs) ranged between 0.5 and 1 cm$^2$ and differed according to the size and morphology of the meningioma. ADC value was measured from three ROIs to calculate the mean ADC in order to minimise variability. The mean ADC of the tumour was also divided by the ADC of the normal white matter that was chosen from distant, normal brain tissue, and was considered to be unaffected by the tumour when determining the normalised ADC (NADC) ratio. Grade II and III meningiomas were grouped together and compared with grade I meningiomas.

The statistical difference between the mean ADC value

**Table.** Characteristics and findings of 28 patients.

| Patient No. | Age (years) | Sex | Location of mass | Pathology | DWI (signal intensity) | ADC value (x $10^{-3}$ mm$^2$/s) | NADC ratio |
|---|---|---|---|---|---|---|---|
| 1 | 61 | Female | Cerebral convexity | Chordoid meningioma, grade II | Mixed | 0.4210 | 0.5329 |
| 2 | 62 | Male | Parasagittal | Atypical meningioma, grade II | Hyperintense | 0.6390 | 0.8171 |
| 3 | 63 | Male | Cerebral convexity | Atypical meningioma, grade II | Mixed | 0.9963 | 1.3391 |
| 4 | 67 | Female | Parasagittal | Atypical meningioma, grade II | Mixed | 0.6223 | 0.7626 |
| 5 | 64 | Male | Parasagittal | Malignant meningioma, grade III | Mixed | 0.7243 | 0.9077 |
| 6 | 69 | Male | Cerebral convexity | Atypical meningioma, grade II | Mixed | 0.6680 | 0.7804 |
| 7 | 70 | Female | Cerebral convexity | Atypical meningioma, grade II | Hyperintense | 0.8480 | 1.1070 |
| 8 | 71 | Male | Parasagittal | Atypical meningioma, grade II | Hyperintense | 0.6670 | 0.9120 |
| 9 | 44 | Female | Cerebral convexity | Meningothelial, grade I | Hyperintense | 0.7683 | 1.0030 |
| 10 | 45 | Female | Sphenoid wing | Meningothelial, grade I | Mixed | 0.8316 | 1.0280 |
| 11 | 46 | Female | Tentorial cerebelli | Meningothelial, grade I | Hyperintense | 0.8163 | 0.9405 |
| 12 | 48 | Female | Olfactory groove | Fibroblastic, grade I | Mixed | 0.7496 | 0.8914 |
| 13 | 49 | Female | Planum sphenoidale | Meningothelial, grade I | Mixed | 1.1553 | 1.4246 |
| 14 | 50 | Female | Floor of anterior cranial fossa | Meningothelial, grade I | Mixed | 0.9236 | 1.2186 |
| 15 | 51 | Female | Parasellar | Meningothelial, grade I | Isointense | 0.8286 | 0.9996 |
| 16 | 52 | Female | Planum sphenoidale | Meningothelial, grade I | Hyperintense | 0.8987 | 1.1967 |
| 17 | 53 | Female | Sphenoid wing | Transitional, grade I | Mixed | 1.2683 | 1.6732 |
| 18 | 54 | Female | Planum sphenoidale | Meningothelial, grade I | Hyperintense | 0.7487 | 0.8365 |
| 19 | 55 | Female | Parasellar | Fibroblastic, grade I | Mixed | 0.7543 | 1.0044 |
| 20 | 56 | Male | Parasagittal | Meningothelial, grade I | Mixed | 0.7747 | 1.0714 |
| 21 | 57 | Male | Olfactory groove | Meningothelial, grade I | Hyperintense | 0.7177 | 0.9582 |
| 22 | 58 | Male | Cerebral convexity | Meningothelial, grade I | Mixed | 0.4933 | 0.6083 |
| 23 | 59 | Female | Cerebello-pontine angle | Transitional, grade I | Mixed | 0.8027 | 0.9173 |
| 24 | 60 | Female | Cerebral Convexity | Fibroblastic, grade I | Mixed | 0.7323 | 1.0143 |
| 25 | 60 | Female | Cerebello-pontine angle | Transitional, grade I | Hyperintense | 0.7450 | 0.8911 |
| 26 | 61 | Female | Cerebello-pontine angle | Meningothelial, grade I | Hyperintense | 0.7877 | 1.0323 |
| 27 | 62 | Male | Cerebral convexity | Angiomatous, grade I | Mixed | 0.7947 | 0.9691 |
| 28 | 63 | Female | Cerebello-pontine angle | Transitional, grade I | Mixed | 1.0063 | 1.3155 |

Abbreviations: ADC = apparent diffusion coefficient; DWI = diffusion-weighted imaging; NADC = normalised apparent diffusion coefficient.

and mean NADC ratio of the benign and atypical / malignant groups of meningioma was assessed using two sample *t* test to determine whether there was a significant difference between the ADC of benign and atypical / malignant groups. A p value of <0.05 was considered statistically significant.

## RESULTS

The DWI findings, ADC value, and NADC ratio with pathological findings of 28 meningiomas are listed in the Table. Of 28 meningiomas, 20 (71.4%) were grade I, 7 (25.0%) were grade II, and 1 (3.6%) was grade III. Meningothelial meningioma was the most common subtype of grade I meningioma (12/20 = 60%) followed by transitional (4/20 = 20%), fibroblastic (3/20 = 15%), and angiomatous (1/20 = 5%). Atypical meningioma was the most frequent subtype of meningioma grade II (6/7 = 85.7%) with one case of chordoid meningioma (1/7 = 14.3%), and one case of meningioma grade III with anaplastic subtype.

The visual inspection of DWI revealed mixed signal intensity in 17 (60.7%) of 28 meningiomas, isointense signal intensity in 1 (3.6%) meningioma, and hyperintense signal intensity in 10 (35.7%) meningiomas. Of 20 grade I meningiomas, 12 (60%) were mixed signal intensity, 1 (5%) was isointense, and 7 (35%) were hyperintense. Of eight grade II, III meningiomas, five (62.5%) were mixed signal intensity and three (37.5%) were hyperintense. The signal characteristics of meningiomas on DWI varied and there was no significant difference in both groups.

The mean ADC value of high-grade meningiomas (0.698 x $10^{-3}$ $mm^2/s$ ± 0.06 x $10^{-3}$ $mm^2/s$) was significantly lower ($p < 0.05$) compared with grade I meningiomas (0.83 x $10^{-3}$ $mm^2/s$ ± 0.37 x $10^{-3}$ $mm^2/s$) [Figures 1 to 3]. The mean NADC ratio of the atypical and malignant type (0.895 ± 0.09) was also lower than the benign type (1.05 ± 0.05) but without statistical significance (p = 0.06).

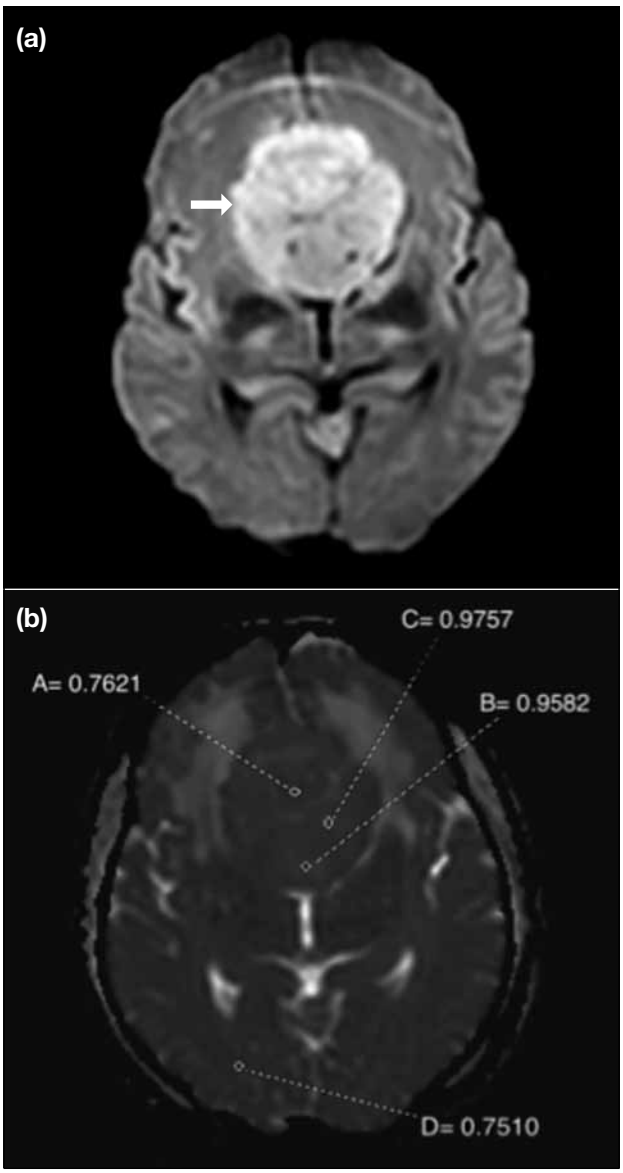


**Figure 1.** Patient No. 16: planum sphenoidale meningothelial meningioma (grade I) in a 52-year-old woman. (a) Diffusion-weighted imaging reveals predominant hyperintensity with regions of mixed signal intensity (arrow). (b) The mean apparent diffusion coefficient (ADC) value measured from three regions of interest (A, B, and C) was 0.8987 x $10^{-3}$ $mm^2/s$. The normalised ADC value with reference to the normal white matter (D) was 1.1967.

Using a mean ADC of less than 0.8 x $10^{-3}$ $mm^2/s$ as a predictor of high-grade meningioma gave a sensitivity of 75% (95% confidence interval, 34.9-96.8), specificity of 65% (40.8-84.6), positive predictive value of 46.2% (19.2-74.9), and negative predictive value of 86.7% (59.5-98.3).

## DISCUSSION

DWI is a non-invasive assessment of tumour cellularity because cellular and subcellular elements significantly impede the mobility of water molecules, thus densely cellular regions exhibit low ADC. Compared with benign meningiomas, atypical and malignant meningiomas have increased mitotic activity and higher nucleus-to-cytoplasmic ratio, contributing to decreased extracellular space, thus more severe restriction of net water diffusion.[6] Many studies have reported that the mean ADC values of benign meningioma are higher

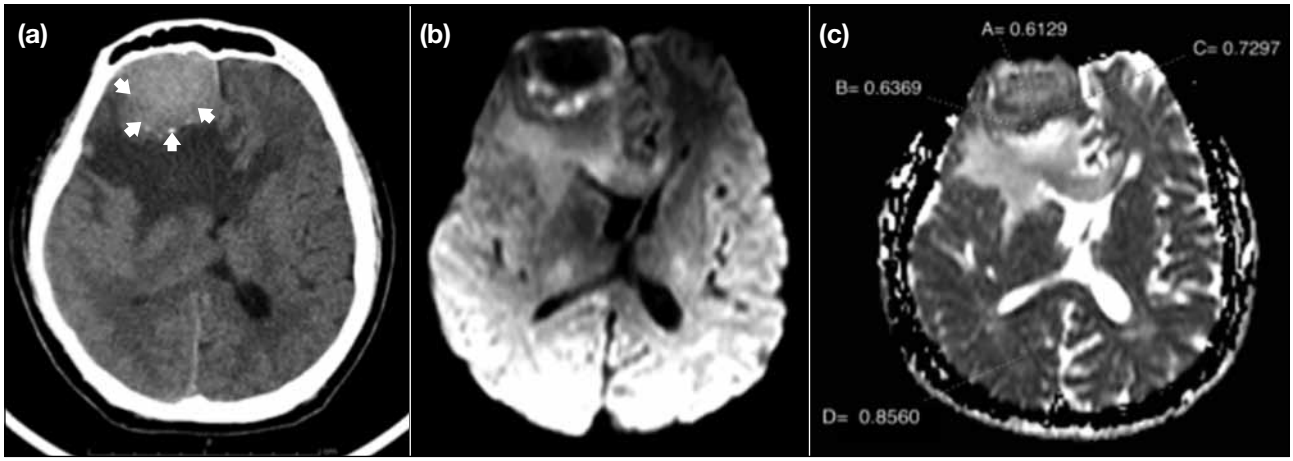


**Figure 2.** Patient No. 6: atypical meningioma (grade II) at right frontal pole in a 69-year-old man with (a) large area of central calcification confirmed by plain axial computed tomographic scan (arrows). (b) Diffusion-weighted imaging reveals large area of central hypointense signal surrounded by peripheral mixed signal intensity. (c) The mean apparent diffusion coefficient (ADC) value measured from three regions of interest (A, B, and C) in the peripheral area without calcification was 0.6680 x $10^{-3}$ $mm^2/s$. The normalised ADC value with reference to the normal white matter (D) was 0.7804.

than the mean ADC values of atypical/malignant meningioma.[2,5-7,9]

Our results were in agreement with previous studies that report a significant statistical difference in ADC value of atypical / malignant and benign meningiomas.[2,5-7,10] The mean ADC value of atypical and malignant meningiomas in our study was significantly lower compared with that of benign meningiomas (0.698 x $10^{-3}$ $mm^2/s$ ± 0.06 x $10^{-3}$ $mm^2/s$ vs. 0.83 x $10^{-3}$ $mm^2/s$ ± 0.37 x $10^{-3}$ $mm^2/s$). Despite some overlap of the ADC values in both benign and atypical / malignant groups, using a mean ADC value of less than 0.8 x $10^{-3}$ $mm^2/s$ as a predictor of high-grade meningioma gave a sensitivity of 75% and specificity of 65%. This finding also concurs with the previous study by Nagar et al[9] that reported an optimal cutoff for a mean ADC value of 0.8 x $10^{-3}$ $mm^2/s$ but with much better sensitivity at 96% and specificity at 82.6% for the differentiation of benign and atypical / malignant meningiomas.

Since the measurement of ADC values may vary across different scanners, DWI sequences, and hardware configurations, the NADC ratio has been recommended to minimise the differences in ADC values caused by different diffusion techniques or sequences. The mean NADC ratio in our study was also lower in the atypical / malignant group than benign group (0.895 ± 0.09 vs. 1.05 ± 0.05) but without statistical significance (p = 0.06). Nagar et al,[9] however, reported the optimal cutoff for a mean NADC of 0.99 with high sensitivity of 96% and specificity of 100% for the differentiation of benign and atypical / malignant meningiomas. We found variability and inconsistency in the determination of the base ADC value of 'normal-looking white matter' that may have contributed to errors and discrepancies.

The ADC value of our single case of chordoid meningioma (WHO grade II) revealed the lowest ADC value, possibly due to associated haemorrhage confirmed by computed tomography. Despite an attempt to avoid the haemorrhagic portion, some paramagnetic susceptibility effects upon the ADC value were inevitable. This was the only meningioma with haemorrhage in our study. Haemorrhage associated with meningiomas is rare. Some risk factors have been described, including patient factors (e.g. age <30 or >70 years, patient on anticoagulant medications) and tumour-related factors such as tumoural infarction or some pathological tumour subtypes (fibrous, atypical, or anaplastic meningiomas).[11]

Female predominance in our study population (19/28 = 67.9%), including the benign group (16/20 = 80%), was noted and expected in meningioma. Nonetheless, male gender was predominant in the atypical / malignant group (5/8 = 62.5%; patients 1 to 8 in the Table), which was statistically significant as determined by

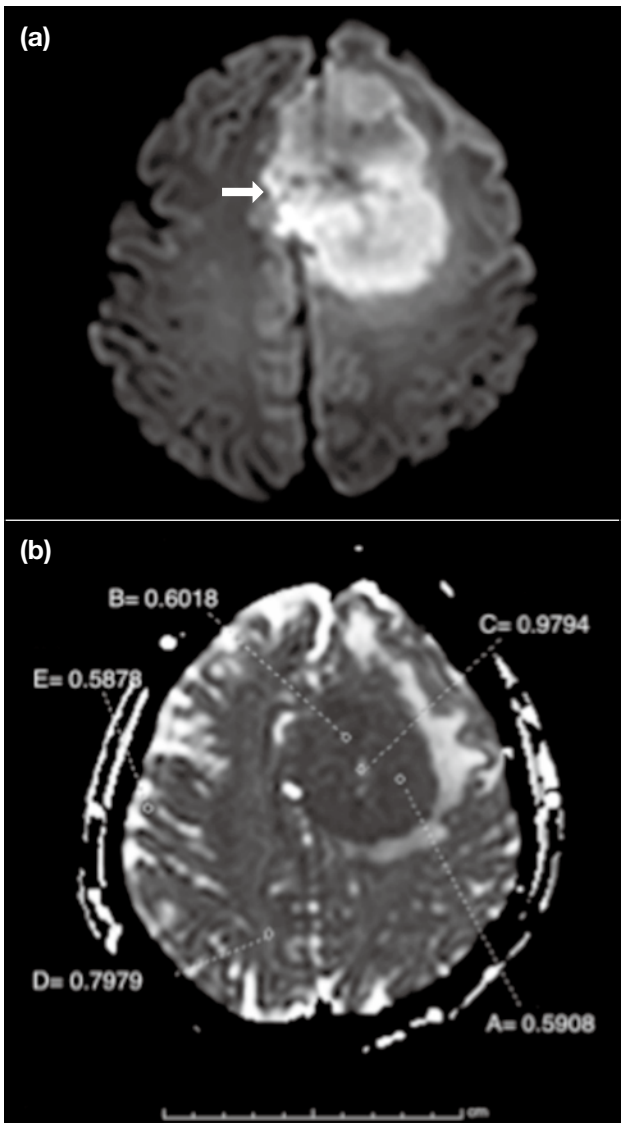


**Figure 3.** Patient No. 5: malignant meningioma (grade III) at the parasagittal region of left frontal lobe in a 64-year-old man. (a) Diffusion-weighted imaging reveals mixed signal intensity (arrow). (b) The mean apparent diffusion coefficient (ADC) value measured from three regions of interest (A, B, and C) was 0.7243 x $10^{-3}$ $mm^2/s$. The normalised ADC value with reference to the normal white matter (D) was 0.9077.

Pearson's chi-square test ($p < 0.05$), and in agreement with previous knowledge that males are predominant in atypical and malignant meningiomas.[12]

Peritumoural oedema has been reported to be unhelpful in differentiating benign meningioma from atypical / malignant meningioma.[2,13] On pathological evaluation, the peritumoural brain tissue showed only extracellular fluid accumulation.[14]

The visual inspection of DWI revealed variable signal intensity in both groups of meningiomas. The majority of meningiomas in our study revealed mixed signal intensity (67.9%), and no significant differences in signal intensity in both groups from our study and also from previous reports.[2,9,13] Furthermore, the visual inspection of the DWI signal for grading meningiomas may also be affected by the T2 shine-through effect. Thus quantitative analysis of the ADC value is suggested and ADC value measurement on the routine PACS workstation can be used conveniently by the radiologist to provide additional information and help predict the grading of meningioma.

The rather small sample size in both groups was the main limitation of our study. Another limitation was that both radiologists reviewed all the studies together and interpreted the images by consensus, resulting in a lack of interobserver variability assessment.

## CONCLUSION

The ADC value measured on PACS of atypical and malignant meningiomas was statistically significantly lower than that of benign meningiomas, and similar to values measured on the dedicated specialised workstation. The PACS offers a convenient and helpful method to predict high-grade meningioma with considerable sensitivity and specificity.

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