

Original Article

Preoperative Assessment and Prediction of Consistency of Intracranial Meningioma Utilizing the Apparent Diffusion Coefficient Values

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Abstract	Objectives Consistency of meningioma is important for preoperative planning, surgical resection, and predicting surgical outcomes. We prospectively evaluated the utility of the apparent diffusion coefficient (ADC) values to assess the consistency of meningioma. Methods Preoperative magnetic resonance imaging (MRI) was performed on 23 patients with meningioma before undergoing surgical resection and the average/mean of ADC minimum (ADC _{min}), maximum (ADC _{max}), and mean (ADC _{mean}) values were calculated. Intraoperatively, the meningiomas were characterized as firm or soft and correlated with ADC values. Results ADC _{min} , ADC _{max} , and ADC _{mean} values of soft and firm meningiomas were significantly different with a <i>p</i> -value of < 0.05. ADC _{min} value of < 691.3 × 10 ⁻⁶ mm ² /s had 80% sensitivity and 84.6% specificity for identifying firm from the soft tumors with
	the area under the curve (AUC) = 0.862, <i>p</i> -value of 0.004, positive predictive value (PPV) 80, and negative predictive value (NPV) 84.6. ADC _{max} value of $< 933.6 \times 10^{-6}$ mm ² /s had 70% sensitivity and 84.6% specificity for identifying firm from the soft tumors with AUC = 0.823, <i>p</i> -value of 0.009, PPV 77.8, and NPV 78.6. ADC _{mean} value
Keywords	of $<$ 840.8 $ imes$ 10 ⁻⁶ mm ² /s had 90% sensitivity and 76.9% specificity for identifying firm
 meningioma 	from the soft tumors with AUC $=$ 0.900, <i>p</i> -value of 0.001, PPV 75, and NPV 90.9.
► ADC	Conclusion Diffusion-weighted MRI using ADC minimum, ADC maximum, and ADC
► surgery	mean values can be used to differentiate firm from soft meningiomas. Meningiomas
 intracranial 	with hard consistency showed relatively low ADC values.

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Introduction

Meningiomas are dural-based tumors that arise from arachnoid cells surrounding the brain.¹ About 90% of meningiomas are supratentorial and seen in the parasagittal region, convexities, sphenoid ridge, and olfactory groove in descending order of frequency. Infratentorial meningiomas are commonly located in clival regions.² petrous and These may become or detected asymptomatically. symptomatic Meningiomas are usually isointense on both T1weighted (T1W) and T2-weighted (T2W) images to the cerebral cortex on magnetic resonance imaging (MRI) with avid enhancement on postcontrast images. Dural tail and vasogenic edema are also commonly seen.³ Surgery is the main modality to treat symptomatic patients with meningioma. The intraoperative consistency of meningioma is vital in formulating the plan of surgical approach and predicting the surgical outcome. Soft consistency tumors can be treated by suctioning whereas those with hard consistency require meticulous prolonged dissection with the added risk of damage to vital structures in the proximity to the tumor. The surgeon needs to have a noninvasive method that can preoperatively evaluate the consistency of meningioma for optimal risk assessment and patient management. Soft tumors can thus be directly approached and treated with suctioning whereas other options such as preoperative transarterial embolization to soften tumors and aid resection can be given in the case of hard meningiomas.⁴

Few studies have employed standard T1W and T2W imaging for preoperative assessment of the consistency of meningioma; however, it remains imprecise because in addition to water content other factors also come into play in defining the consistency of tumor.^{5–8} A previous study by Yogi et al⁹ has retrospectively demonstrated a significant correlation between the apparent diffusion coefficient (ADC)_{min} values and intraoperative tumor consistency. The primary intention of our study was to evaluate the utility of ADC values in preoperative prediction of consistency of meningioma and comparing with intraoperative assessment by the neurosurgeon.

Materials and Methods

This was a single-institution prospective study that was approved by the Institute Ethics Committee of our institute. A total of 23 consecutive meningioma patients who were operated on during the study period of January 2015 to May 2016 were enrolled in the study. The risks and possible benefits of the procedure were fully explained to the patients and written informed consent was taken from the patient before enrollment in the study as per the attached pro forma. Inclusion criteria were surgical candidates of meningioma referred for preoperative MRI. Exclusion criteria were the presence of MRI acquisition contraindications, metallic implants, that is,

claustrophobia, refusal to give consent, meningioma which was showing more than 50% areas of necrosis or calcification, and recurrent/residual meningioma.

All MR examinations were performed on a 1.5 T MR scanner-Magnetom Aera system (Siemens Healthcare, Erlangen, Germany)-using a quadrature head coil. All patients underwent MRI including T1W imaging sequence (repetition time [TR]/echo time [TE]) [ms] = 1890/4.17; section thickness, 1 mm); and axial turbo spin-echo T2W imaging sequence ([TR/TE] [ms] = 4290/109; section thickness, 4mm). Susceptibility-weighted imaging (SWI) sequence was acquired in the axial plane (TR/TE) (ms) = 49/40; section thickness, 2.2 mm. Diffusionweighted imaging (DWI) was acquired in the axial plane using single-shot spin-echo echo-planar (EP) sequences (field of view, 230 mm; section thickness, 4 mm; intersection gap, 2.5 mm; acquisition time, 70s; and b values, 0 and 1,000 s/mm²) with subsequent generation of ADC maps.

The MRI-DWI data set was transferred to a workstation and systematically evaluated by a neuroradiologist with over 3 years of experience. The observer who was blinded to the patient's details created the manual regions-of-interests (ROIs) along the tumor border on T2WI. This ROI was then brought on to ADC map. The observer ensured to avoid areas with necrosis and calcification within the ROI. Areas of cystic degeneration and susceptibility artifacts derived from nearby air and bone structures were avoided. The ADC minimum, ADC maximum, and ADC mean values were generated from ROI. ROIs were drawn on all slices where the lesion was visualized. Mean of ADC minimum (ADC_{min}), mean of ADC maximum (ADC_{max}), and mean of ADC mean (ADC_{mean}) were calculated. Necrosis was defined as the presence of T2 heterogeneous hyperintensity in the tumor which does not show contrast enhancement. Calcification was defined as the presence of a T2 hypointense area that shows blooming on SWI.

Operative technique: For all patients, surgical resection was done by a neurosurgeon who was blinded to the consistency based on imaging parameters and classified them into two groups: "soft" consistency (removed predominantly by suction) and "firm" consistency (predominantly excised) according to Sitthinamsuwan et al criteria.¹⁰

Statistical analyses: The statistical analysis was done by SPSS software version 20 (Statistical Packages for the Social Sciences, Chicago, Illinois, United States). The Kolmogorov– Smirnov test was done to determine the normality of data distribution. Quantitative variables like age and ADC values were calculated and presented as mean \pm standard deviation (SD). For categorical data (soft/hard, malignant/benign, male/female, presence or absence of symptom) number and the percentage were calculated. Cronbach's α reliability test was used to measure the intraobserver variability of ADC values by ROI. The comparison between consistency of meningioma and ADC values (minimum, maximum, and mean) were done by using a Student's *t*test because ADC values are normally distributed. A receiver operating characteristic (ROC) curve was used to calculate cutoff points of ADC value to differentiate soft from hard tumors with calculations of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of this diagnostic tool. A *p*-value of < 0.05 was considered to indicate statistical significance.

Results

The study population consisted of 18 (78.3%) females and 5 (21.7%) males with a mean age of 47.17 years (SD: 10.391, range o29-68 years). The anatomical distribution of meningiomas includes three along the sphenoid ridge, one in the cerebellopontine angle, eight along the cerebral convexity, five in the parasagittal location, two in the tuberculum sellae, two along the tentorium, one along the cribriform plate, and one in the petroclival region. ADC_{min}, ADC_{max}, and ADC_{mean} value of soft and firm meningiomas were significantly different. ADC_{min} value of ${<}\,691.3 \times 10^{-6} \ mm^2/s$ had 80% sensitivity and 84.6% specificity for identifying firm from the soft tumors with area under the curve (AUC) = 0.862, p-value of 0.004, PPV 80, and NPV 84.6 (\succ Figs. 1 and 2). ADC_{max} value $of\,{<}\,933.6\,{\times}\,10^{-6}~mm^2/{s}$ had 70% sensitivity and 84.6% specificity for identifying firm from the soft tumors with AUC = 0.823, p-value of 0.009, PPV 77.8, and NPV 78.6 (**Figs. 3** and **4**). ADC_{mean} value of $< 840.80 \times 10^{-6} \text{ mm}^2/\text{s}$ had 90% sensitivity and 76.9% specificity for identifying firm from the soft tumors with AUC = 0.900, *p*-value of 0.001, PPV 75, and NPV 90.9 (**-Figs. 5** and **6**). Cronbach's α reliability test showed excellent consistency of ADC values by ROI (ADC_{min} 0.975, ADC_{max} 0.985, and ADC_{mean} 0.987). At surgery, 10 meningiomas were classified as hard and 13 as soft. On histopathology, the soft group (- Fig. 7) consisted of six meningothelial, five transitional, one angiomatous, and one chordoid subtypes. The hard group (Fig. 8) consisted of seven meningothelial, two fibroblastic, two angiomatous, and one secretory meningioma subtypes. Out of 23



Fig. 1 Box and whisker plot showing the correlation between consistency of the meningioma and the average minimum apparent diffusion coefficient (ADC)_{min} value.



Fig. 2 Average Minimum Apparent diffusion coefficient (ADC)_{min} value of $< 691.3 \times 10^{-6}$ mm²/s giving 80% sensitivity and 84.6% specificity for identifying firm from the soft tumors with area under the curve (AUC) = 0.862. *p*-Value is 0.004, positive predictive value (PPV) 80, and negative predictive value (NPV) 84.6.



Fig. 3 Box and whisker plot showing the correlation between consistency of the meningioma and the average maximum apparent diffusion coefficient (ADC)_{max} value.



Fig. 4 Average Maximum Apparent diffusion coefficient (ADC)_{max} value of $< 933.6 \times 10^{-6}$ mm²/s giving 70% sensitivity and 84.6% specificity for identifying firm from the soft tumors with area under the curve (AUC) = 0.823. *p*-Value is 0.009, positive predictive value (PPV) 77.8, and negative predictive value (NPV) 78.6.



Fig. 5 Box and whisker plot showing the correlation between consistency of the meningioma and the Average mean apparent diffusion coefficient (ADC)_{mean} value.



Fig. 6 Average mean Apparent diffusion coefficient (ADC)_{mean} value of $< 840.80 \times 10^{-6}$ mm²/s giving 90% sensitivity and 76.9% specificity for identifying firm from the soft tumors with area under the curve (AUC) = 0.900. *p*-Value is 0.001, positive predictive value (PPV) 75, and negative predictive value (NPV) 90.9.

meningiomas, 21 were benign (World Health Organization [WHO] grade I) and 2 were atypical (WHO grade II). No correlation was found between the ADC values and WHO grading of meningioma.

Discussion

The intraoperative consistency of meningioma is vital for planning the surgical strategy, predicting the degree of removal, and adjunctive therapy. Differentiation of soft from firm tumors will be useful in early surgical planning. Previously, few studies have shown the correlation between MR signal and meningioma consistency. Sitthinamsuwan et al¹⁰ showed that the signal intensity of meningiomas on T2WI and fluid-attenuated inversion recovery images were independent factors and significantly correlate with its consistency. Hoover et al¹¹ retrospectively included 101 patents with intracranial meningioma to characterize based on T1/T2 signal intensities. They concluded that and T2WI series can predict meningioma T1WI consistency with overall sensitivities for detecting soft and firm consistency as 90 and 56%, respectively. Maiuri et al⁷ found in their study that meningiomas showing increased hyperintensity than the cortex on T2WI were usually soft whereas those with hypointensity were frequently hard. But few other studies did not demonstrate such an association between MRI signal intensity and consistency.^{12,13} The consistency of meningioma as in any tumor is based on cellularity and amount of fibrous tissue. In cases of meningioma, there is the presence of interdigitations that



Fig. 7 A 42-year-old woman with meningothelial meningioma in left tentorium region. The tumor shows hyperintensity on T2 weighted image (T2WI) (A), hypointensity on T1WI (B), and slight hyperintensity on diffusion-weighted imaging (DWI) (C). The region-of-interest (ROI) was drawn around the tumor on the apparent diffusion coefficient (ADC) map (D). The calculated ADC_{min}, ADC_{max}, and ADC_{mean} values were 779.3 × 10⁻⁶ mm²/s, 964 × 10⁻⁶ mm²/s, and 872.4 × 10⁻⁶ mm²/s, respectively. The ADC_{min}, ADC_{max}, and ADC_{mean} values were above the cutoff values (691.3 × 10⁻⁶ mm²/s, 933.67 × 10⁻⁶ mm²/s, 840.8 × 10⁻⁶ mm²/s, respectively). Total removal was performed and the consistency was classed as soft.

are connected with extracellular cisterns and junctional complexes. Increased cellularity and fibrous contents can result in low T2W signal, while the presence of widened extracellular space with increased interstitial fluid can cause high T2W signal intensity. Thus, there is a complex interplay between these factors which may limit the utility of conventional sequences to predict the consistency of meningioma. Studies done previously also suggested that the ADC value inversely correlates with fibrous tissue content and cellularity.^{8,14,15} Thus, it is assumed that the tumors with low ADC value may have a hard consistency. At present, there are only a few studies that established the ability of DWI in the preoperative characterization of intracranial meningiomas. We tried to compare the ADC_{min}, ADC_{max}, and ADC_{mean} values of meningiomas among soft and firm groups. In our study, when using ADC_{min} value of $< 691.33 \times 10^{-6}$ mm²/s for identification of hard tumors, it shows 80% sensitivity and 84.6% specificity with AUC = 0.862, *p*-value of 0.004, PPV 80, and NPV 84.6. When using ADC_{max} value of $< 933.67 \times 10^{-6}\ mm^2/s$ for identification of the hard tumors, it shows 70% sensitivity and 84.6% specificity with AUC = 0.823, *p*-value of 0.009, PPV 77.8, and NPV 78.6. When using ADC_{mean} value of $< 840.8 \times 10^{-6}$ mm²/s giving 90% sensitivity and 76.9%



Fig. 8 A 46-year-old woman with a meningothelial meningioma at left sphenoid ridge. On T2 weighted image (T2WI) (A), the tumor shows hyperintensity. The tumor shows slight hypointensity to isointensity on T1WI (B). The tumor shows hyperintensity on diffusion-weighted imaging (DWI) (C). The region-of-interest (ROI) was drawn around the tumor on apparent diffusion coefficient (ADC) map (D). The calculated ADC_{min}, ADC_{max}, and ADC_{mean} values were 676 × 10⁻⁶ mm²/s, 921 × 10⁻⁶ mm²/s, and 799.2 × 10⁻⁶ mm²/s, respectively. The ADC_{min}, ADC_{max}, and ADC_{mean} values were below the cutoff values (691.3 mm²/s, 933.67 mm²/s, 840.8 mm²/s, respectively). Total removal was performed and the consistency was classed as hard.

specificity for identifying firm from the soft tumors with AUC = 0.900, *p*-value of 0.001, PPV 75, and NPV 90.9. Hoover et al found no correlation in their study with ADC and tumor consistency; however, they did not calculate ADC values and only qualitative analysis was performed.¹¹ Watanabe et al found no correlation between the ADC value and meningioma consistency. They believed that the ADC value is affected not only by the extracellular volume fraction but also by tumor cellularity.¹⁶

A study performed in meningiomas by Yogi et al⁹ showed that hard meningiomas compared with soft meningiomas has significantly lower ADC_{min} value (p0.001). But, ADC_{max} and ADC_{mean} values showed no significant difference between the two groups, though these values of the hard group are likely to be lower (p = 0.52 and 0.21, respectively). According to the ADC_{min} value, the ROC curve had shown 0.64×10^{-3} mm²/s as the best cutoff value in their study. According to this cutoff value, sensitivity and specificity were 88 and 81%, respectively, and the AUC was 0.9. These values are similar to the values of our study except for mild differences. Besides, ADC_{max} and ADC_{mean} values also showed a significant difference between firm and soft groups in our study. This may be due to the inherent

difference in the study composition of the meningiomas encountered in the two studies and the differences in the study protocol and anatomical location. We intentionally avoided areas of cystic degeneration and susceptibility artifacts. Similar to previous studies our study also evaluated the correlation between ADC values and histopathological subtypes but found no significant association.¹⁷⁻¹⁹

Multiple studies have demonstrated the association between ADC values and meningioma grades with atypical and malignant meningiomas showing lower ADC values as compared with benign meningiomas.^{20,21} We could not find any correlation between ADC values and WHO grading of meningioma, likely due to predominant study population (21 out of 23) had benign/WHO grade I meningiomas. There were few limitations in our study. The sample size in our study was relatively small. Further studies with a larger sample size are needed to know the exact diagnostic accuracy of DWI. No histopathological correlation was found with ADC values with this small sample size. DWI was on echo planar sequences which are highly susceptible to artifacts especially at the skull base and along the air sinuses.

Conclusion

Diffusion-weighted MRI using ADC minimum, ADC maximum, and ADC mean values can be used to differentiate firm from soft meningioma. Meningiomas with low ADC values are considered to have a hard consistency. DWI is a basic sequence available in most MRI scanners and the findings are easily reproducible. We promise that this quick and easily applied system using ADC can be used to predict the intraoperative consistency of cranial meningioma on preoperative MRI. It is vital to know the consistency of meningioma for proper surgical planning and utilization of devices to minimize the complication and improve surgical outcomes.

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Conflict of Interest None declared.

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