The Role of Diffusion-weighted Magnetic Resonance Imaging in the Evaluation of Brain Mass Lesions

Ravi Ningappa, Bagath Singh K, Santosh Kumar P Uppinal, Nagaraj BR

Department of Radiodiagnosis, Victoria Hospital, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India

Correspondence: Dr. Ravi Ningappa, Associate Professor, Department of Radiodiagnosis, Victoria Hospital Bangalore Medical College and Research Institute, Bangalore - 560 040, Karnataka, India. E-mail: raviningappa6@gmail.com

ABSTRACT

Context: The purpose of this study was to assess the role of diffusion-weighted-magnetic resonance imaging (DW-MRI) and apparent diffusion coefficient (ADC) values in the evaluation of different benign and malignant brain mass lesions with histopathological correlation. **Aims:** To assess the role of DW-MRI in the evaluation of different mass lesions of the brain with histopathological correlation. To evaluate the role of ADC values in characterization and differentiation of benign and malignant mass lesions of the brain. **Settings and Design:** The study design was a cross-sectional study and it was done in patients who were referred to Victoria Hospital attached to Bangalore Medical College and Research Institute (BMC and RI), Bengaluru between December 2012 and November 2014. The sample size of the study was 50. **Subjects and Methods:** We retrospectively reviewed 50 MR examinations of patients who were referred to Department of Radio Diagnosis, BMC, and RI, Bengaluru for intracranial mass lesion evaluation with MRI. All of them had undergone conventional MRI examination with Siemens AVANTO 1.5T scanner, and we determined ADC values and signal intensities on DW images (DWIs). In all patients with contrast-enhanced tumors, region of interests (ROIs) were placed in the enhanced region. In patients with nonenhancing tumors, ROIs were placed in the solid part of the lesion. We also evaluated the correlation between ADC values and cellularity in the mass lesions. Additional clinical details and histopathological findings were correlated with the DWI and ADC findings for radiologic-pathologic concordance. **Statistical Analysis:** Brain MRI results of 50 patients with histologically verified or clinically diagnosed brain mass lesions were subjected to analysis. They ranged in age from 2 to 72 years (mean, 43.5 years). The examinations were performed with a 1.5T scanner, an 8-channel surface head coil. The examination protocol included the following sequences and images: Turbo spin-echo (SE) T2-weighted images (3920/102/1), fluid-attenuated inversion recovery (2500/9000/111/1) ([inversion time/repetition time (TR)/echo time (TE)/excitations], and SE T1-weighted images [488/10/1] [TR/TE/excitations]), carried out in three planes, before and after contrast medium administration (in a standard dose). **Results:** A positive correlation was found in the comparison of mean ADC values for high-grade gliomas (1.19×10^{-3} mm²/s ± 0.2) and metastasis (0.833×10^{-3} mm²/s ± 0.2), low-grade gliomas (1.34×10^{-3} mm²/s ± 0.2), and medulloblastomas (0.68×10^{-3} mm²/s ± 0.075), as well as for in epidermoid cyst and necrotic areas in malignant tumors. **Conclusion:** ADC is useful in the differentiation of various brain mass lesions, in grading brain tumors, and differentiation of benign cystic and malignant necrotic areas. The combination of routine image interpretation and ADC had a higher predictive value. The ADCs of glioma, metastasis, and meningioma are related to tumor cellularity. We believe that DWIs and ADCs can provide information useful to diagnose brain mass lesions that cannot be obtained with conventional MRI alone.

Key words: Apparent diffusion coefficient; brain mass lesion; diffusion-weighted imaging; magnetic resonance

Introduction

A conventional magnetic resonance imaging (MRI) examination allows for visualization of a mass lesion, and provides us with information on mass location,

Access this article online	
Quick Response Code:	Website: www.wajradiology.org
	DOI: 10.4103/1115-1474.164875

How to cite this article: Ningappa R, Singh KB, Uppinal SP, Nagaraj BR. The role of diffusion-weighted magnetic resonance imaging in the evaluation of brain mass lesions. West Afr J Radiol 2016;23:76-81.

its homogeneity and signal intensity, the presence of perilesional edema, and degree of contrast enhancement. Among the brain mass lesions, differentiation between low and high-grade tumors based on MRI is still very difficult. Traditional tumors of high-grade are very heterogeneous, which results from the presence of necrotic and/or hemorrhagic regions, an extensive vascular edema, strong enhancement, and mass effect. However, these signs are not always present. Sometimes, low-grade tumors show features typical for more malignant tumors.[1,2] Similarly, differentiation between intracerebral necrotic tumors and cerebral abscesses is frequently impossible with conventional MRI.

Diffusion-weighted imaging (DWI) is a very well-known and a widely used method, present in a routine MRI protocol, and allowing for evaluation of a normal brain tissue or its lesions caused by ischemia, injury, proliferation, multiple sclerosis, or abscess.[3-7]

Our hypothesis was that DWIs and mass lesion apparent diffusion coefficient (ADC) could provide additional useful information in the differential diagnosis of patients with brain mass lesions and differentiation between intracerebral necrotic tumors and other benign cystic lesions.

The aim of the work was to evaluate the usefulness of ADC in differentiation of various brain mass lesions and also establishing the grade of brain tumors with direct information on cellular density of tumors and differentiation of benign cystic and malignant necrotic areas.

Subjects and Methods

The study design was a cross-sectional study, and it was carried out on patients who were referred to Victoria Hospital attached to Bangalore Medical College and Research Institute, Bengaluru between December 2012 and November 2014. The sample size of the study was 50.

Inclusion criteria

- Patients referred with features suggestive of brain masses based on the clinical data or other imaging modality
- Cases were included irrespective of age/sex.

Exclusion criteria

- Contraindications to MRI studies, such as patients with pacemakers, metallic implants, and aneurysmal clips
- Claustrophobia or anxiety disorders exacerbated by MRI
- Not willing to give consent.

Methods

Brain MRI results of 50 patients with histologically verified or clinically diagnosed brain mass lesions were subjected to analysis. They ranged in age from 2 to 72 years (mean, 43.5 years). The examinations were performed with a 1.5T scanner, an 8-channel surface head coil. The examination protocol included the following sequences and images: Turbo spin-echo (SE) T2-weighted imaging (3920/102/1), fluid-attenuated inversion recovery (FLAIR) (2500/9000/111/1) ([-inversion time/repetition time [TR]/echo time (TE)/excitations], and SE T1-weighted images (488/10/1) [TR/TE/excitations]), carried out in three planes, before and after contrast medium administration (in a standard dose). Matrix: 256 × 256 and 256 × 192, field of view: 220–230 mm, slice thickness: 3–5 mm, and slice interval of 30%.

DWI was performed before contrast medium administration; sequence parameters – TR/TE-2300/73, field of view: 230 mm, matrix: 128 × 128, slice thickness: 5 mm, slice interval: 1 mm, and *b*-values 0/500/1000 mm^2/s. The DWIs were acquired by using the echo-planar imaging (EPI) sequence that combined the motion-probing gradient before and after the 180° pulse with EPI readout and fat was suppressed by placing a frequency-selective RF pulse before the pulse sequence.

ADC was measured with a manual placement of region of interests (ROIs) in the solid part of the lesion. The solid part of the lesion was identified on the basis of a detailed analysis of T1-weighted images after contrast administration and T2-weighted images, including FLAIR sequence. In case of enhancing tumors, ROIs were placed in the enhanced region, while in case of nonenhancing tumors; ROIs were placed in the solid part of the lesion, identified on the basis of a FLAIR image.

The measurements were taken 3 times and included calculation of a mean value for each lesion. ROI size was 5 pixels (approximately 50–100 mm^2).

The measurements did not include cystic, necrotic, hemorrhagic areas, or edema surrounding the tumor.

Results

Thirteen gliomas (five high-grade glioma - WHO III/IV and eight low-grade glioma WHO I/II), 10 metastatic tumors, 9 meningiomas, 7 schwannomas, 3 abscesses, 3 epidermoid cysts, 3 hemangioblastomas, and 2 medulloblastomas (WHO IV) were included in our study.

Among high-grade tumors, ADC values ranged from 1.012 to 1.315 × $10^{-3}mm^2/s$. In low-grade tumors, ADC values ranged from 1.09 to 1.78 × 10^{-3} mm^2/s. Among metastasis, ADC values ranged from 0.56 to 1.074 × 10^{-3} mm^2/s. In meningioma, ADC values ranged from 0.72 to 1.14 × 10^{-3} mm^2/s. In schwannoma, it was 0.877–1.32 × 10^{-3} mm^2/s. In the group of medulloblastomas, it was 0.51–0.86 × 10^{-3} mm^2/s. In hemangioblastomas, it was 0.978–1.429 × 10^{-3} mm^2/s. Among benign cystic lesions in the epidermoid cyst, ADC values ranged from 0.79 to 0.98 × 10^{-3} mm^2/s and in abscess it was 0.425–0.603 × 10^{-3} mm^2/s [Table 1].

A positive correlation was found in the comparison of mean ADC values for high-grade gliomas (1.19×10^{-3} mm^2/s ± 0.2) and metastasis (0.833×10^{-3} mm^2/s ± 0.2), low-grade gliomas (1.34×10^{-3} mm^2/s ± 0.2) and medulloblastomas (0.68×10^{-3}mm^2/s ± 0.075), as well as for epidermoid cyst and necrotic areas in malignant tumors.

Discussion

MR diffusion imaging has been used to study water mobility in normal brain tissue, cerebral infarction, multiple sclerosis, gliomas, and brain abscesses, and to differentiate between arachnoid cysts and epidermoid cysts and other diseases.[6,8] Preoperative differentiation of brain mass lesions is very important, due to different therapeutical approaches and prognosis.

Table 1: Distribution of ADC values in various benign and malignant brain Mass Lesions

Tumor type	No of patients	Age range (years)	ADC Range (X10^{-3}mm^2/sec)	Mean ADC (X10^{-3}mm^2/sec)
High grade glioma	5	11-64	1.012-1.315	1.193
Low grade glioma	8	12-62	1.090-1.788	1.342
Metastasis	10	33-72	0.565-1.074	0.833
Meningioma	9	39-63	0.720-1.147	0.874
Schwanomma	7	24-60	0.877-1.320	1.039
Hemangioblastomas	3	18-48	0.978-1.429	1.220
Medulloblastoma	2	7-18	0.511-0.861	0.686
Epidermoid cyst	3	33-50	0.797-0.984	0.910
Abscess	3	2-41	0.425-0.603	0.503

ADC – Apparent diffusion coefficient

Differentiation of mass lesions such as tumors with a standard MRI, on the basis of such criteria as: Signal intensity of the mass lesion, presence of cysts, necrotic regions, peri-tumoral edema, as well as the degree of contrast enhancement or its lack, is unreliable or even impossible.[9] Both in the literature and in our material, the malignant mass lesions were not always enhancing after contrast administration, the peri-tumoral edema was not always present, and the cysts and/or necrotic regions were present in both malignant, and in benign tumors.[9] That is why; it is required to search for other, modern imaging methods, which would be helpful in the differentiation of the brain mass lesion.

On imaging studies, malignant gliomas usually are enhanced after intravenous contrast injection and show peritumoral edema, whereas, except for pilocytic astrocytoma and giant-cell astrocytoma, low-grade gliomas usually show little to no abnormal enhancement or peritumoral edema. Differentiation of these two types of tumors occasionally may be difficult, because low-grade astrocytomas also may show abnormal contrast enhancement and peritumoral edema. In fact, the abnormal enhancement was noted in three of eight patients with low-grade astrocytoma in our study, and peritumoral edema was found in four patients.

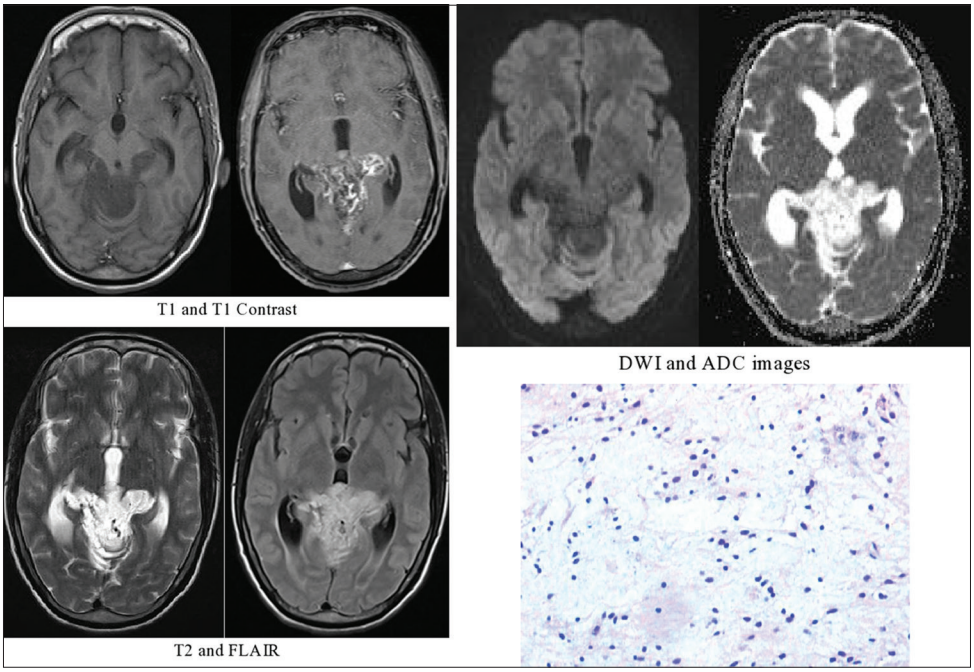

Figure 1: T1-weighted images, T2-weighted images, fluid-attenuated inversion recovery, T1-weighted images contrast, diffusion-weighted imaging apparent diffusion coefficient mapping, and histopathology. 42-year-old male presented with difficulty while walking since 6 months and now complaints of swaying while walking, diminished vision, and headache since 2 months. Ill-defined infiltrative heterogeneously enhancing T1-weighted images hypointense, T2-weighted images/fluid-attenuated inversion recovery hyperintense lesion involving the pineal gland and tectal plate region causing obstructive hydrocephalus. Diffusion-weighted imaging and apparent diffusion coefficient map (mean apparent diffusion coefficient: 1.788×10^{-3} mm^2/s). Diagnosis: Post third ventricular tumor - Pilocytic astrocytoma. Histopathology slide: HPE shows sheets of bipolar pilocytic astrocytes with rosenthal fibres and reactive vessel proliferation

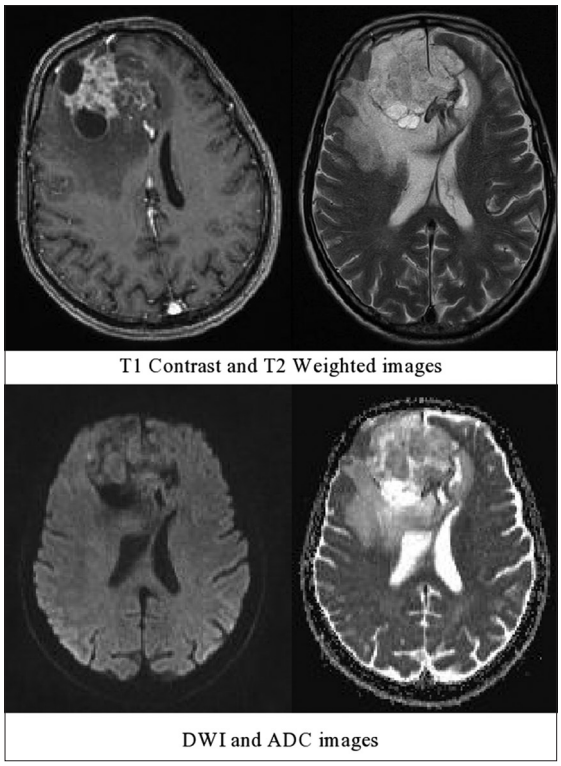

Figure 2: Glioblastoma multiforme. 56-year-old male presents with serve headache, giddiness, and vomiting since 3 months. Magnetic resonance imaging shows an ill-defined intraaxial enhancing mass T1-weighted images hypointense (not shown here). T2-weighted images hyperintense lesion with multiple blooming on gradient images with cystic lesions within seen in the right frontal lobe. The enhancing solid portion of the lesion shows restriction on diffusion-weighted imaging (men apparent diffusion coefficient of 0.44 × 10^{-3} mm^2/s). Biopsy report: Glioblastoma multiforme

We found that ADC values cannot be used in individual cases to differentiate tumor types reliably. Although the ADCs of Grade II astrocytoma and glioblastoma overlapped somewhat, the combination of routine image interpretation and ADC had a higher predictive value. Our results indicated that lower ADCs suggest malignant glioma, whereas higher ADCs suggest low-grade astrocytoma. These results agree with those of previous reports.[10] Although no patients with anaplastic astrocytoma were included in our study, we expect that the ADCs of this type of tumor (a Grade III astrocytoma) will be intermediate between those of glioblastoma and Grade II astrocytoma.

A standard differentiation of brain tumors with T2-weighted images shows some differences in signal intensity of the lesions. FLAIR sequence is less useful in the differential diagnosis.

Astrocytomas reveal higher signal intensity in T2-weighted images, but not as high as the cerebrospinal fluid. Pilocytic astrocytomas frequently show much higher signal intensity than medulloblastomas. This concerns both the cystic and the solid part of astrocytomas. Differences in signal intensity are directly connected with the histological structure of the tumors. Malignant tumors with high mitotic activity are

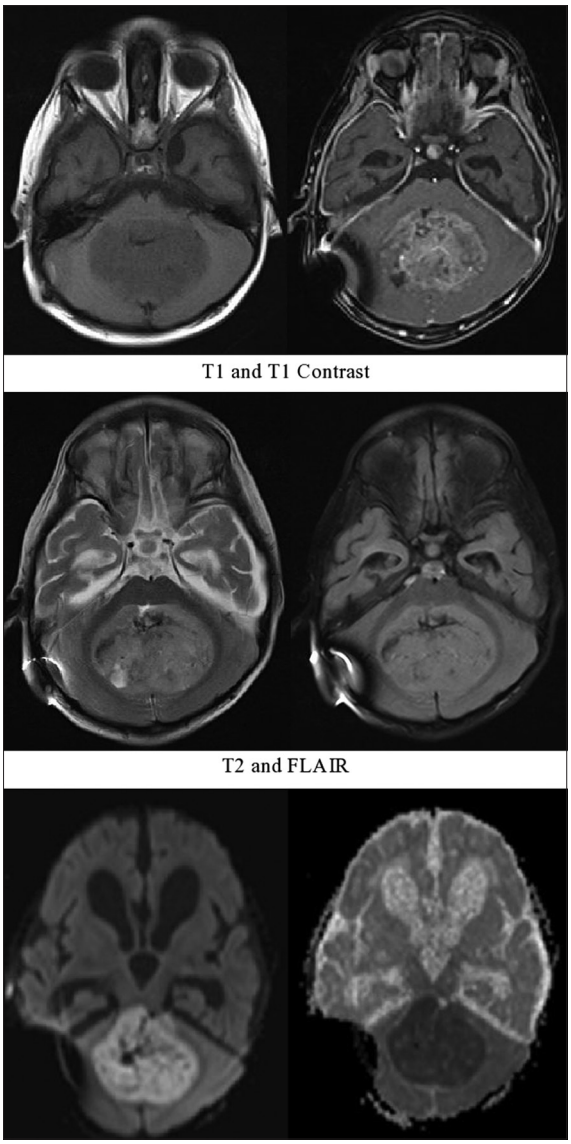

Figure 3: T1-weighted images, T1-weighted images contrast, T2-weighted images, fluid-attenuated inversion recovery, diffusion-weighted imaging, and apparent diffusion coefficient mapping. 7 years aged male child presents with a history of increase in the size of head since 6 months. Also, c/o blurring of vision, weakness of upper and lower limbs, unable to walk with high-stepping gait with one episode seizure. Magnetic resonance imaging shows a large well defined T1-weighted images hypointense and T2-weighted images/ fluid-attenuated inversion recovery iso to hyperintense, heterogeneously enhancing lesion in the fourth ventricle showing restriction on diffusion-weighted imaging (mean apparent diffusion coefficient of 0.511 × 10^{-3} mm^2/s). Biopsy report: Medulloblastoma - WHO Grade IV

hypercellular and reveal lower signal intensity than benign tumors with a looser structure.

In typical medulloblastomas, the solid part of the tumor is isointense in comparison to the gray matter. This is connected with a higher ratio between the nuclei and the cytoplasm in tumor cells, that is, reduction of free water molecules in this region. The observed tumor heterogeneity, on the other hand, is the result of formation of small cysts and calcifications.

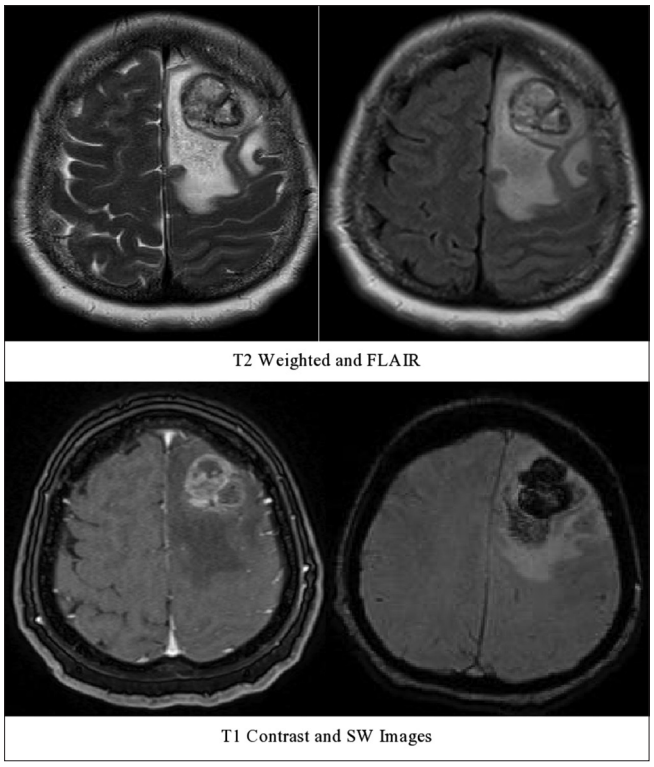

Figure 4: T1 Contrast, SWI, T2 Weighted, FLAIR, DWI and ADC mapping 49 Years female presented with headache since 7 days sudden in onset severe in intensity, more on the left frontal region which relieved on taking medication, history of weakness in right upper limb, difficulty in combing hair and mixing food. A fairly-defined intra axial enhancing lesion with multiple central hyperintensities on T2 weighted images and surrounding peritumoral edema in the left high frontal lobe showing diffusion restriction in the peripheral enhancing solid portion of the lesion on DW images (mean ADC: 0.81 $\times 10^{-3}$ mm^2/s). HPE Report: Section studied showed features of metastatic papillary adeno carcinoma. Diagnosis: Left frontal metastatic papillary adeno carcinoma

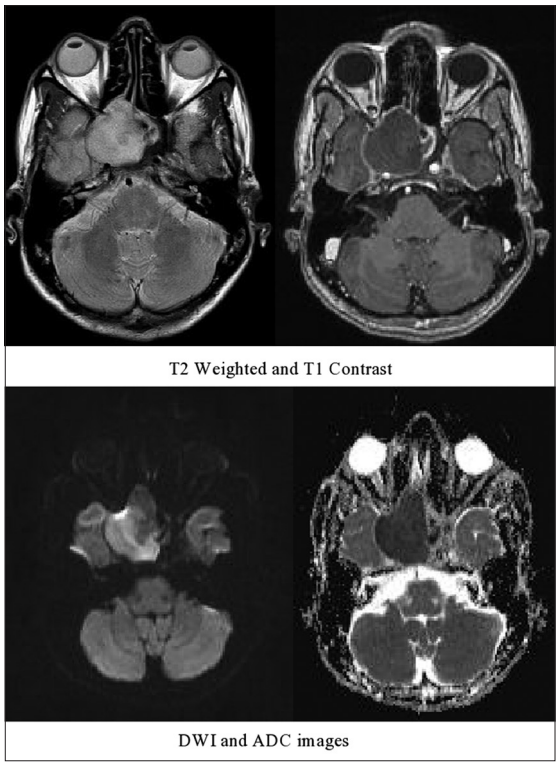

Figure 5: T1-weighted images contrast, T2-weighted images, diffusion-weighted imaging, and apparent diffusion coefficient mapping. 32-year-old male presents with severe headache and vomiting since 3 months. Magnetic resonance imaging shows a well-defined peripherally enhancing T2-weighted images heterogeneous signal intense lesion in the right sphenoid sinus region causing compression of right optic nerve at the apex and shows restriction on diffusion-weighted images (mean apparent diffusion coefficient of 0.444 $\times$ 10^{-3} mm^2/s). Above imaging features suggestive of abscess

DWI is a well-known and a commonly used sequence, which allows for visualization and differentiation of: Ischemic foci in their early phase, dermoid cysts, inflammatory lesions, and proliferative processes of the central nervous system.

This method depends on the degree of free diffusion of water molecules in the examined environment. The extracellular space is characterized by a relative isotropy and a relatively high diffusion coefficient, as in the case of the cerebrospinal fluid present in brain ventricles. The intracellular space reveals anisotropy of a different degree, depending on the number and density of the cell membranes. On the basis of the data obtained from measurements carried out in at least two sequences with a different degree of coefficient *b* (different amplitude and different time of gradient), ADC images are construed, with their values reflecting the degree of diffusion in a given region.

Due to the differences in diffusion rate of water molecules depending on the environment (serum, mucus, pus, solid tissue, etc.), there appeared many publications aiming to evaluate the differences in cellular density of mass lesions, and indirectly also in mitotic activity of the tumors, with the use of diffusion degree within the lesion. In the previously published reports, it was found that an increase in cellular density leads to a higher signal intensity in DWI and a lower effective diffusion coefficient on the ADC map. Published reports have confirmed an inverse relation between the cellular density and the ADC value[5,11-13] In our report, we analyzed various types of brain mass lesions and establish the role ADC in characterization and differentiation of benign and malignant brain mass lesions as well as differentiation between intracerebral necrotic tumors and other benign cystic lesions.

On the basis of ADC evaluation in the presented group of patients, we showed a possibility of differentiation between high grade glioma and metastasis, pilocytic astrocytomas and medulloblastomas, as well as necrotic tumors and benign cystic lesions such as abscess, epidermoid cyst, and arachnoid cyst.

ADC coefficient values for different types of tumors in our patients were similar to the results of the previously published reports.[11,14,15] In most of the cases, ADC was significantly decreased in high-grade tumors of Grade III and Grade IV,

and increased in benign tumors of Grade I (WHO) [Figure 1] and significantly decreased in high-grade tumors of Grade III and Grade IV [Figure 2].

Mean diffusion rate in the solid part of pilocytic astrocytomas amounted in our study to 1.342×10^{-3} mm^2/s, and 0.686×10^{-3} mm^2/s for medulloblastomas [Figure 3].

Similar data were published in 2006, and the mean ADC of tumors in the quoted article amounted to $1.65 \pm 0.27 \times 10^{-3}$ mm^2/s and $0.66 \pm 0.15 \times 10^{-3}$ mm^2/s, respectively.[15]

The ADC of glioblastomas is reportedly lower than that of metastatic tumors.[9] However, our results indicate that the ADC is not useful for differentiating between glioblastomas and metastatic tumors [Figure 4].

In our study, we found ADC measurements to be useful in cases in which a conventional MR was ambiguous or revealed features of infiltration of adjacent structures. An example may be a 42-year-old man with a tumor located in the pineal region, who revealed quite homogeneously increased signal intensity. Standard MRI showed an ill-defined infiltrative lesion in the pineal region causing obstructive hydrocephalus. However, ADC measurements showed a mean diffusion rate within the tumor typical for pilocytic astrocytoma. This was confirmed with a histopathological examination [Figure 1].

Diffusion-weighted MR imaging also was used in the diagnosis of cerebral abscesses and differentiation between necrotic tumors and abscess. In 1996, Ebisu[16] reported a case of brain abscess (Streptococcus intermedius) with a high signal intensity in the abscess cavity on diffusion-weighted images associated with a low ADC value (0.31×10^{-3} mm^2/s). He concluded that diffusion-weighted imaging might enable one to distinguish brain abscesses from cystic or necrotic tumors. In our cases, the mean ADC values in the central part of the abscess were 0.42 and 0.63, respectively [Figure 5].

Our results and the literature support the idea that reduced ADC values in the central part of the abscess are related to the presence of pus. Ebisu[16] also performed an in vivo diffusion-weighted im- aging of aspirated pus, as well as ADC measurements. The pus imaged in vitro showed high signal intensity and very low ADC values, consistent with the results of the in vivo study. He concluded that the pus structure itself is responsible for the low ADC values, and that the heavily impeded water mobility of pus may be related to its high cellularity and viscosity. On the other hand, the cystic or necrotic components of tumors show marked signal suppression on diffusion-weighted MR images, similar to that of CSF, and the calculated ADC values are in the range of $2.2 \pm 0.9 \times 10^{-3}$ mm^2/sec.

Our results of diffusion examined in brain mass lesions showed that a low mean ADC value is most frequent in high-grade tumors, while a high one is more indicative of benign tumors.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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