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Diffusion-Weighted Imaging in Meningioma: Prediction of Tumor Grade and Association with Histopathological Parameters[1,2]

Alexey Surov*, Sebastian Gottschling*, Christian Mawrin†, Julian Prell‡, Rolf Peter Spielmann*, Andreas Wienke§ and Eckhard Fiedler¶

*Department of Radiology, Martin-Luther-University Halle-Wittenberg, Ernst-Grube-Str. 40, 06097 Halle; †Department of Neuropathology, Otto-von-Guericke-University Magdeburg, Leipziger Str. 44, 39120 Magdeburg; ‡Department of Neurosurgery, Martin-Luther-University Halle-Wittenberg, Ernst-Grube-Str. 40, 06097 Halle; §Institute of Medical Epidemiology, Biostatistics and Informatics, Martin-Luther-University Halle-Wittenberg, Magdeburger Straße 8, 06112 Halle; ¶Department of Dermatology (histopathological laboratory), Martin-Luther-University Halle-Wittenberg, Ernst-Grube-Str. 40, 06097 Halle

Abstract

OBJECTIVES: To analyze diffusion-weighted imaging (DWI) findings of meningiomas and to compare them with tumor grade, cell count, and proliferation index and to test a possibility of use of apparent diffusion coefficient (ADC) to differentiate benign from atypical/malignant tumors. *METHODS:* Forty-nine meningiomas were analyzed. DWI was done using a multislice single-shot echo-planar imaging sequence. A polygonal region of interest was drawn on ADC maps around the margin of the lesion. In all lesions, minimal ADC values (ADC_{min}) and mean ADC values (ADC_{mean}) were estimated. Normalized ADC (NADC) was calculated in every case as a ratio ADC_{mean} meningioma/ADC_{mean} white matter. All meningiomas were surgically resected and analyzed histopathologically. The tumor proliferation index was estimated on Ki-67 antigen–stained specimens. Cell density was calculated. Collected data were evaluated by means of descriptive statistics. Analyses of ADC/NADC values were performed by means of two-sided *t* tests. *RESULTS:* The mean ADC_{mean} value was higher in grade I meningiomas in comparison to grade II/III tumors (0.96 vs 0.80 $\times 10^{-3}$ mm^2s^{-1}, $P = .006$). Grade II/III meningiomas showed lower NADC values in comparison to grade I tumors (1.05 vs 1.26, $P = .015$). There was no significant difference in ADC_{min} values between grade I and II/III tumors (0.69 vs 0.63 $\times 10^{-3}$ mm^2s^{-1}, $P = .539$). The estimated cell count varied from 486 to 2091 (mean value, 1158.20 ± 333.74; median value, 1108). There were no significant differences in cell count between grade I and grade II/III tumors (1163.93 vs 1123.86 cells, $P = .77$). The mean level of the proliferation index was 4.78 ± 5.08%, the range was 1% to 18%, and the median value was 2%. The proliferation index was statistically significant higher in grade II/III meningiomas in comparison to grade I tumors (15.43% vs 3.00%, $P = .001$). Ki-67 was negatively associated with ADC_{mean} ($r = -0.61$, $P < .001$) and NADC ($r = -0.60$, $P < .001$). No significant correlations between cell count and ADC_{mean} ($r = -0.20$, $P = .164$) or NADC ($r = -0.25$, $P = .079$) were found.

ADC_{min} correlated statistically significant with cell count ($r = -0.44$, $P = .002$) but not with Ki-67 ($r = -0.22$, $P = .129$). Furthermore, the association between ADCmin and cell count was stronger in grade II/III tumors ($r = -0.79$, $P = .036$) versus grade I meningiomas ($r = -0.41$, $P = .008$). An ADC_{mean} value of less than 0.85 $\times 10^{-3}$ mm^2s^{-1} was determined as the threshold in differentiating between grade I and grade II/III meningiomas (sensitivity 72.9%, specificity 73.1%, accuracy 73.0%). The positive and negative predictive values were 33.3% and 96.8%, respectively. The same threshold ADC_{mean}

Address all correspondence to: Alexey Surov, PhD, MD, Department of radiology, Martin-Luther-university Halle-Wittenberg, Ernst-Grube-Str. 40, 06097 Halle.
E-mail: alex.surow@medizin.uni-halle.de

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value was used in differentiating between tumors with Ki-67 level ≥ 5% and meningiomas with low proliferation index (Ki-67 < 5%). This threshold yielded a sensitivity of 70.6%, a specificity of 81.2%, and an accuracy of 77.6%. The positive and negative predictive values were 66.6% and 83.9%, respectively. *CONCLUSIONS:* Grade II/III tumors had lower ADC_{mean} values than grade I meningiomas. ADC_{mean} correlated negatively with tumor proliferation index and ADC_{min} with tumor cell count. These associations were different in several meningiomas. ADC_{mean} can be used for distinguishing between benign and atypical/malignant tumors.

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Introduction

According to the literature, diffusion-weighted imaging (DWI) provides information regarding tissue microstructure [1–6]. Furthermore, it has been shown that DWI can be used to distinguish malignant from benign tumors [1,4,5]. As reported previously, malignant tumors showed lower apparent diffusion coefficient (ADC) values in comparison to benign lesions [1,3]. In addition, as suggested in previous reports, ADC values under 1.00×10^{-3} mm^2s^{-1} were suspicious for a malignancy [1].

However, according to the literature, some benign lesions had also very low ADC values and can mimic malignancies [7–9]. For example, ADC values of nasopharyngeal adenoid hypertrophy varied from 0.36 to 0.84×10^{-3} mm^2s^{-1} with a median value of $0.59 \pm 0.11 \times 10^{-3}$ mm^2s^{-1} [7]. In addition, in the study of Ikeda et al., the mean ADC of Warthin tumors was significantly lower than that of malignant parotid tumors [8]. Furthermore, it is well known that cholesteatomas also has low ADC values [9].

As reported previously, ADC values correlated well with cell count of the investigated lesions [2,6,9]. For instance, Driessen et al. reported that ADC was significantly and inversely correlated with cell density ($r = -0.57$, $P = .02$) in laryngeal and hypopharyngeal carcinomas [6]. In addition, Schnapauff et al. identified a linear relation between tumor cellularity and ADC in soft tissue sarcoma with a Pearson correlation coefficient of −0.88 [2]. Similar results were reported also for prostatic cancer and renal malignancies [10,11]. However, Wu et al. found no correlation between the ADC value and the tissue cellularity in patients with diffuse large B-cell lymphoma and follicular lymphoma [12]. Furthermore, according to another report, the ADC value for breast cancer did not significantly correlate with cancer cellularity but did correlate with histological types [13].

According to the literature, ADC can be used as a marker to predict response to therapy in different malignant diseases [14–16].

There were several reports describing features of meningiomas on DWI; however, the provided data were inconsistent [17–20]. Whereas some authors found an association between ADC and histological parameters of meningiomas [18,19,21], others did not [17,20]. In addition, in the analysis of Ginat et al., no association between ADC and Ki-67 level was found [22], whereas other authors reported a statistically significant correlation between these parameters [21].

Because of the fact that meningioma is the most frequent intracranial tumor and is often an incidental finding on magnetic resonance imaging (MRI), it is important to correctly estimate tumor grade and proliferation potential on imaging [21].

Therefore, the purpose of this study was to analyze DWI findings of meningiomas and to compare them with different histological parameters such as tumor grade and subtypes, cell count, and proliferation index and to test a possibility of ADC use to differentiate benign from matypical/malignant tumors.

Materials and Methods

This study was approved by the institutional review board (Martin Luther University medical ethic committee).

Patients and Imaging

Images of all meningiomas resected at our institution in the time period from 2006 to 2013 were analyzed retrospectively. Only tumors which were investigated by DWI with good quality of images were included into the study. Tumors below 10 mm in diameter, calcified meningiomas, and tumors with artifacts on DWI/ADC map were excluded from the study. After a thorough inspection of the images, 49 tumors were adopted for further analysis. These tumors were found in 38 women and 11 men with a mean age of 59.0 years (median age, 63 years; range, 20-82 years).

In all patients, MRI of the head was performed using a 1.5-T device (Magnetom Vision Sonata Upgrade, Siemens, Erlangen, Germany). The imaging protocol included axial T2-weighted fat-suppressed short-tau-inversion-recovery images and axial T1-weighted (T1w) spin echo images before and after intravenous application of contrast medium (gadopentate dimeglumine, Magnevist, Bayer Schering Pharma, Leverkusen, Germany). DWI was done using a multislice single-shot echo-planar imaging sequence (repetition time/echo time: 5900/96 milliseconds; field of view: 250 × 250 mm; slice thickness: 5 mm; acquisition matrix: 128 × 128), with b values of 0, 500, and 1000 s/mm^2. ADC maps were automatically generated by the implemented software according to the following equation: ADC (mm^2s^{-1}) = $[\ln(S^0/S^{1000})]$ / 1000, where S^0 and S^{1000} represent the signal intensities of the images. The slice with the largest diameter of meningioma was selected for ADC calculation. In this image. a polygonal region of interest (ROI) as large as possible was manually drawn on ADC maps around the margin of the lesion (whole lesion measurement) without risking partial volume effects. ROIs were placed to avoid cystic and necrotic areas as well as large vessels of the tumors. The position of every ROI was automatically placed also on all other images (T2 weighted, and pre- and postcontrast T1w). In all lesions, minimal ADC values (ADC_{min}) and mean ADC values (ADC_{mean}) were estimated. In addition, ROIs were drawn in the normal white matter of the contralateral hemisphere (ADC white matter). Normalized ADC (NADC) was calculated in every case as a ratio ADC_{mean} meningioma/ADC_{mean} white matter.

All images were analyzed retrospectively by one radiologist (A.S., 11 years of radiological experience).

Histopathological Analysis

All 49 meningiomas were surgically resected and analyzed histopathologically. Tumor grading was classified according to the World Health Organization [23].