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CASE REPORT

Spatial Restriction within Intracranial Epidermoid Cysts Observed Using Short Diffusion-time Diffusion-weighted Imaging

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We report two cases of pathologically proven intracranial epidermoid cysts. Both cases were scanned with diffusion-weighted imaging using pulsed gradient spin-echo (PGSE) and oscillating gradient spin-echo (OGSE; 50 Hz) prototype sequences with diffusion times of 47.3 ms and 8.5 ms, respectively. The apparent diffusion coefficient measured by OGSE was higher than that measured by PGSE, indicating the spatial restriction of water diffusion in the laminated keratin layers within the cyst as demonstrated by histopathology.

Keywords: *diffusion-weighted imaging, oscillating gradient spin-echo, restricted diffusion, tissue microstructure, epidermoid cyst*

Introduction

The apparent diffusion coefficient (ADC) in diffusion-weighted imaging (DWI) strongly depends on the effective diffusion time (Δ_{eff}), which is the time allowed for water molecules to diffuse and probe the local environment *in vivo*. Increasing Δ_{eff} allows the molecules to interact with more barriers, thus decreasing the ADC value, which eventually reaches an asymptotic lower value.[1,2] The diffusion time was shown to be the key element enhancing the contrast of an acute cerebral infarction case on DWI.[3] Thus, the Δ_{eff}-dependence of ADC values may provide insight into microstructural information, including compartment size and diffusivity, cell membrane permeability, and the nuclear-to-cell ratio.[1,4] An oscillating gradient spin-echo (OGSE) sequence was proposed to substantially reduce the diffusion time.[1,2,4] A study by Colvin et al.[5] reported the benefit of OGSE in revealing the intracellular structure (i.e., the nuclear size of glioblastoma) in an *in vivo* rat model. Wu et al.[4] also showed that OGSE can be used to differentiate the molecular layer from the granule cell layer in the adult mouse cerebellum. Further, Reynaud et al.[6] demonstrated that OGSE at moderately high frequencies (65–225 Hz) can be used to disentangle structural restriction and free diffusivity in a murine glioma model.

Case Reports

The cases of two women are included in this report. The two patients were a 31-year-old woman (patient I) and a 20-year-old woman (patient II) with chief complaints of right trigeminal neuralgia and left peripheral vision loss, respectively. Both patients were scanned on a 3T magnetic resonance (MR) scanner (MAGNETOM Prisma; Siemens Healthcare, Erlangen, Germany) with a 20-channel head coil. Lesions with typical characteristics of epidermoid cysts[7] were observed on MR images of the cerebellopontine angle and suprasellar region in patients I and II, respectively.

DWI was performed with prototype sequences using b-values of 0 and 1500 s/mm^2 (number of excitations one and four, respectively) and three diffusion-encoding directions for each pulsed gradient spin-echo (PGSE) (Δ_{eff} = 47.3 ms; diffusion gradient pulse duration [δ], 41.3 ms; diffusion gradient separation [Δ], 57.1 ms) and OGSE with trapezoid-sine

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waveforms[8] (frequency = 50 Hz; Δ_{eff} = 8.5 ms; δ = 7.1 ms; Δ = 50 ms) (Fig. 1). Other parameters were as follows: repetition time (TR), 4600 ms; echo time (TE), 120 ms; field-of-view, 200 × 200 mm^2; matrix size, 72 × 72; slice thickness, 4 mm; and acquisition time, 1-min and 16-s for PGSE and 1 min and 33 s for OGSE.

Regions of interest (ROIs) 0.4 cm^2 in size were placed within the epidermoid cysts on the ADC maps (Fig. 1). ROIs were placed carefully to avoid partial-volume effects from adjacent brain tissue and cerebrospinal fluid (CSF). ROIs were also placed in the centrum semiovale and in the fourth ventricle to determine the ADC values of white matter (WM) and CSF, respectively.[9] The mean ADC values of epidermoid cysts, WM, and CSF are shown in Table 1.

Histopathology of both cases revealed a squamous epithelial lining with laminated layers of keratin filaments and flakes within the cysts (Fig. 2). The distance between two layers of keratin was approximately 10–25 μm.

Discussion

Intracranial epidermoid cysts arise from the inclusion of ectodermal elements during neural tube closure.[7] Histopathologically, the epidermoid cyst is lined by a thin wall of stratified squamous epithelium with the formation of concentric lamellae of keratin filling the interior of the cyst due to the continuous accretion of keratin debris.[7] Epidermoid cysts typically show high signal intensity on DWI.[7] The ADC values of epidermoid cysts were reported to be lower than those of CSF and higher than those of brain tissue.[10] Therefore, whether the observed signal changes in epidermoid cysts on DWI is due to diffusion restriction or T_2 shine-through remains controversial.[11]

DWI is mainly performed using PGSE diffusion encoding, which has a large Δ_{eff}.[2] For this reason, restriction effects caused by increased intracellular viscosity are indistinguishable from those of increased diffusion barriers at spatial

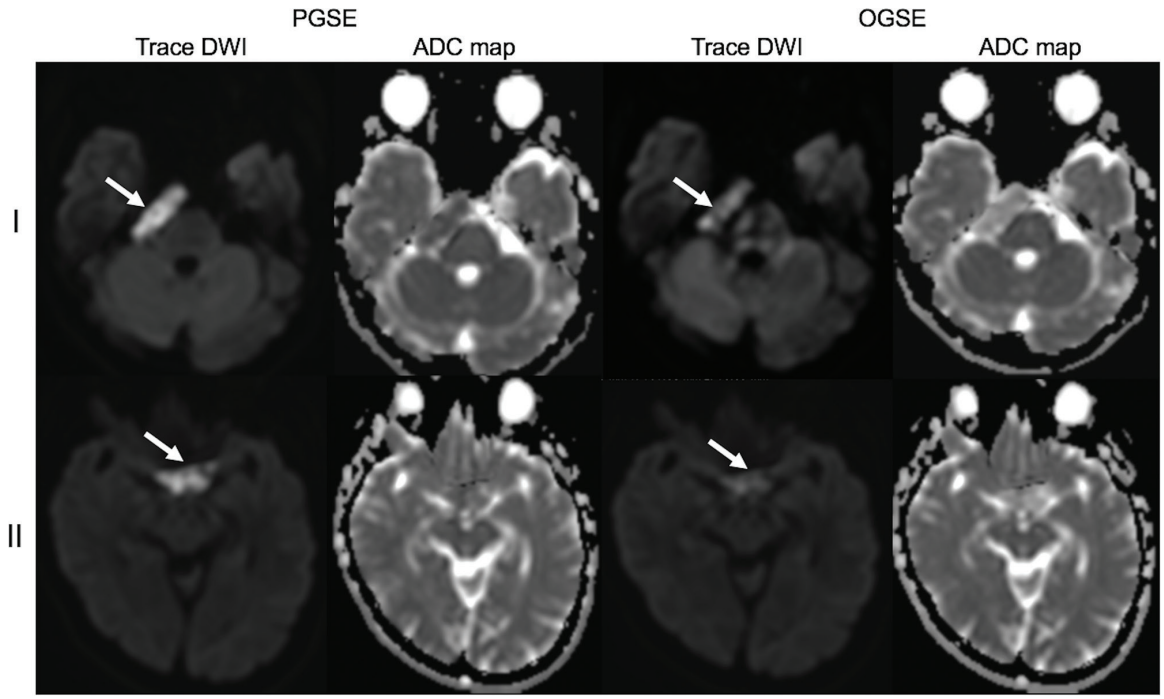

Fig. 1 Diffusion-weighted imaging (DWI) of epidermoid cysts from patients I and II. Each column displays images in the following order: pulsed gradient spin-echo (PGSE) trace DWI, PGSE apparent diffusion coefficient (ADC) map, oscillating gradient spin-echo (OGSE) trace DWI, and OGSE ADC map. Epidermoid cysts (arrows) appear as hyperintense lesions on PGSE and OGSE DWI. ADC maps show a lower ADC on PGSE and a higher ADC on OGSE.

Table 1 Apparent diffusion coefficient (ADC) measurements in the pulsed gradient spin-echo (PGSE) and oscillating gradient spin-echo (OGSE) sequences. The values are expressed in 10^{-3} mm^2/s ± standard deviation

ADC value	Patient I		Patient II	
	PGSE	OGSE	PGSE	OGSE
Epidermoid cyst	0.69 ± 0.07	1.26 ± 0.05	0.79 ± 0.08	1.25 ± 0.08
White matter	0.62 ± 0.02	0.69 ± 0.01	0.63 ± 0.03	0.69 ± 0.04
Cerebrospinal fluid	2.58 ± 0.43	2.64 ± 0.43	2.82 ± 0.30	2.84 ± 0.32

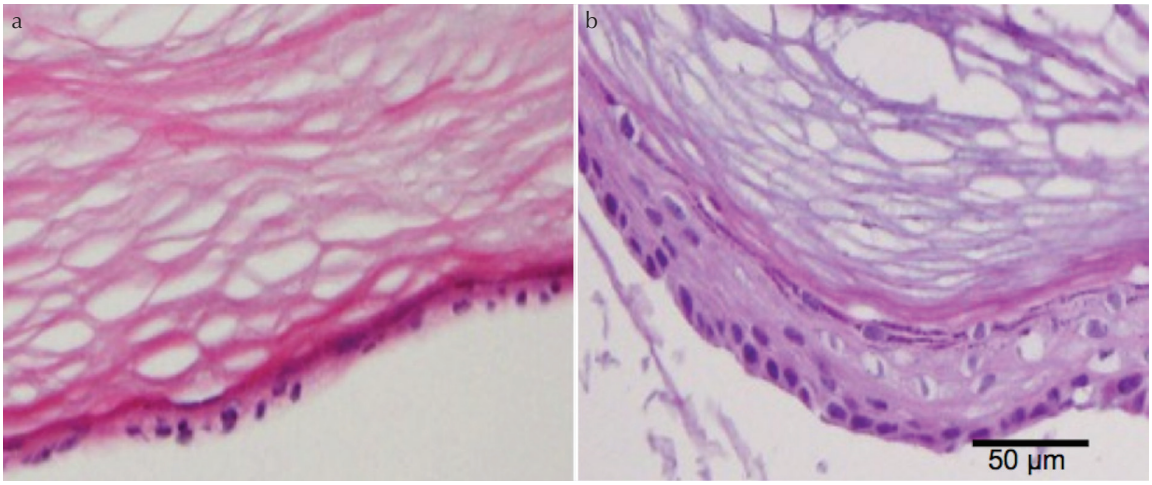

Fig. 2 Photomicrographs of epidermoid cysts with a squamous epithelial lining from patients I (**a**) and II (**b**) are shown. Laminated keratin layers separated by interstitium are seen beneath the epithelial lining. Hematoxylin and eosin (H&E) stain, ×200.

scales that can only be probed at shorter diffusion times.[6] With the availability of sequences like OGSE that enable short diffusion-weighting periods, it is possible to reduce Δ_{eff}.[1] Therefore, OGSE bears the potential to filter diffusion MRI signals based on the sizes of the underlying microstructural barriers.[4,6]

In the current report, the epidermoid cysts showed higher ADC values at shorter diffusion times compared to those at longer diffusion times. The Δ_{eff} values used in this study were 47.3 ms for the PGSE sequence and 8.5 ms for the OGSE sequence, yielding mean square distances (x^2) of water molecule diffusion in the direction perpendicular to the keratin layers of 16.85 μm and 7.14 μm, respectively (considering a diffusion coefficient of 3×10^{-3} mm^2/s at body temperature).[4] Assuming that the range of x^2 values (7.14–16.85 μm) observed with ADC changes represents the average distance between barriers, relatively good agreement was found with the average distance between keratin layers (10–25 μm) shown by the histopathology measurements. However, the keratin layers were expected to be more dense *in vivo*, not only because of their progressive production but also because artifacts, such as cell shrinkage and the separation of cell layers from each other, may affect the tissue specimen during the fixation process.[12] In comparison, WM and CSF were shown to have similar ADC values with both PGSE and OGSE sequences. Note that the Δ_{eff} employed in the present study was relatively long. Baron et al.[1] showed that Δ_{eff} less than 7 ms, which corresponds to an x^2 of 4.6 μm, is needed to observe the dependence of ADC on diffusion times in the white matter. Meanwhile, no restricted diffusion is expected within the CSF.

The observed time dependence of the ADC may reflect the restriction of water diffusion due to the concentric layers of keratin filaments within the cyst, thus limiting the movement of water molecules to planes formed between the two layers of keratin. These findings are in line with diffusion tensor metrics from previous studies that demonstrated disc-like anisotropy within epidermoid cysts, representing diffusion in the geometric plane that is spanned by the two largest eigenvalues ($\lambda_1 \sim \lambda_2 >> \lambda_3$) rather than in a single direction as in the case of white matter ($\lambda_1 >> \lambda_2 \sim \lambda_3$).[11]

Conclusion

In the present study, two cases of intracranial cysts were analyzed with DWI using PGSE and OGSE (50 Hz) sequences. The diffusion time dependence of the ADC (a lower ADC value at a longer Δ_{eff} and a higher ADC value at a shorter Δ_{eff}) observed in the epidermoid cysts suggests spatial restriction of the water molecules' diffusion between the keratin layers within the cysts. Further studies with a larger number of patients incorporating acquisitions at additional frequencies will likely provide greater insight into the microstructure of epidermoid cysts to estimate the packing correlation length and tissue diffusivity. Moreover, future research should increase the number of motion-probing gradient directions to observe directional differences in time-dependent behavior.

Conflicts of Interest

Thorsten Feiweier is an employee of Siemens Healthcare GmbH, Erlangen Germany and Katsutoshi Murata is an employee of Siemens Healthcare K.K., Japan. All remaining authors declare no conflicts of interest associated with this manuscript.

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