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INNOVATIVE CLINICAL IMAGE

Time-dependent Diffusion in Brain Abscesses Investigated with Oscillating-gradient Spin-echo

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Oscillating-gradient spin-echo sequences enable the measurement of diffusion weighting with a short diffusion time and can provide indications of internal structures. We report two cases of brain abscess in which the apparent diffusion coefficient (ADC) values appear higher at short diffusion times in comparison with those at long diffusion times. Diffusion time dependence of the ADC in brain abscesses suggests not only substrate viscosity but also restricted diffusion due to the structure within the lesions.

Keywords: *brain abscess, diffusion-weighted imaging, diffusion time, microstructure, oscillating-gradient spin-echo*

Innovative Clinical Image

Oscillating-gradient spin-echo (OGSE) sequences can shorten diffusion times by replacing the long-lasting diffusion-sensitizing gradients used in pulsed-gradient spin-echo (PGSE) methods with rapidly oscillating gradients.[1–3] Recently, the OGSE sequence has become available on clinical MRI scanners. If most molecules do not move far enough to interact with any obstacle during the preset diffusion time, the apparent diffusion coefficient (ADC) is the intrinsic diffusion coefficient of cellular water. As the diffusion time increases, molecules interact with more barriers, and the observed ADC decreases asymptotically. Therefore, it is expected that diffusion-weighted imaging (DWI) with the OGSE sequence can estimate the substrate's viscosity and spatially restricted diffusion, based on the internal structures of the lesions, from changes in the ADC values with different diffusion times.[4–6]

A brain abscess is an accumulation of pus in the brain due to infection. Brain abscesses are characterized by a markedly high signal on DWI. It is speculated that the high signal in a brain abscess is due to viscosity.[7–9]

We showed that alkanes (C_nH_{2n+2}), which are viscous liquids, are useful as isotropic diffusion phantoms and that the ADC values of alkanes do not depend on diffusion times.[10] If the high signal on DWI of brain abscesses is due to viscosity, the ADC values should not change even if the diffusion time is changed. To estimate the internal structures of brain abscesses, we investigated the ADC values of brain abscesses scanned with shorter diffusion times using a prototype OGSE DWI sequence, complemented by a conventional scan with a PGSE DWI sequence.

The case of a 39-year-old woman (patient 1) with post-treatment of maxillary sinus cancer and that of a 5-year-old girl (patient 2) with a history of cardiac surgery are reported here. Patient 1 had two brain abscesses (brain abscesses I and II), and patient 2 had one brain abscess (brain abscess III). The brain abscess of patient 1 was drained. The culture showed infection with fusobacterium nucleatum, and the brain abscess was pathologically diagnosed. The brain abscess of patient 2 was drained, the culture showed microaerophilic streptococcus infection, and the brain abscess was diagnosed by intraoperative findings. The patients underwent scanning with a 3 T MR scanner (MAGNETOM Prisma; Siemens Healthcare, Erlangen, Germany) using a 20-channel head/neck coil. Diffusion tensor imaging (DTI) was performed with prototype sequences using b-values of 0 and 1000 s/mm^2 and six uniformly distributed directions for both OGSE and PGSE acquisitions. OGSE, using a trapezoid-cosine waveform[11], was performed with an effective diffusion time (Δ_{eff}) of 6.5 ms (frequency = 30 Hz; diffusion gradient pulse duration [δ] = 7.6 ms), complemented by a PGSE with Δ_{eff} 35.2 ms (diffusion gradient separation

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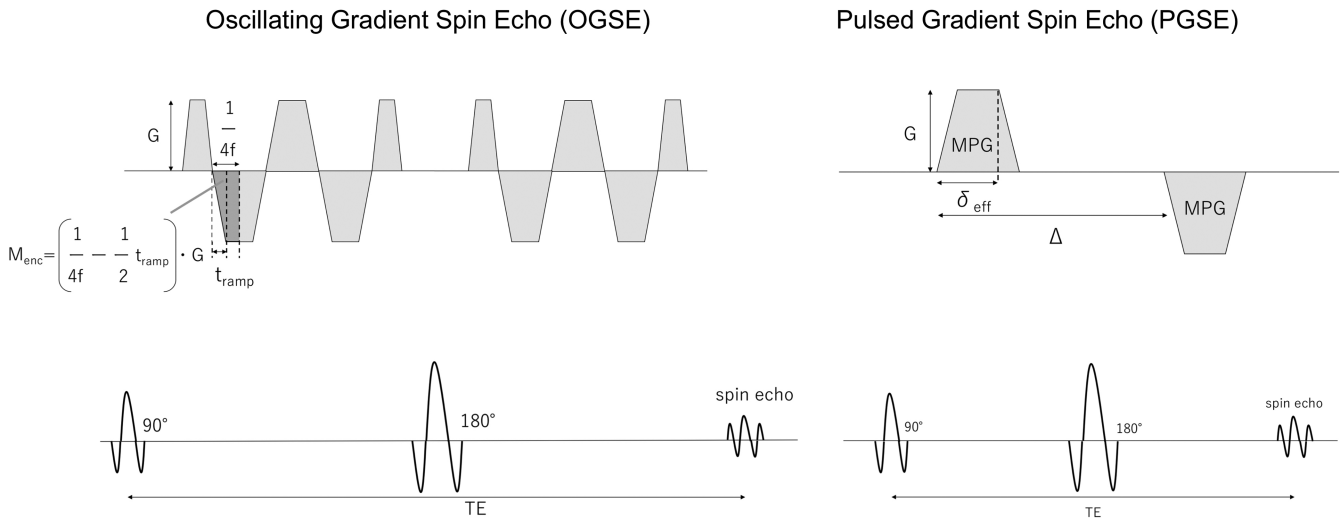

Fig. 1 The pulse sequence diagram for OGSE and PGSE. An OGSE method can shorten the diffusion times by replacing the long diffusion-sensitizing gradients used in PGSE methods with rapidly oscillating gradients. M_{enc} = 0th moment of the first lobe of the oscillating diffusion-encoding gradients; G = maximum gradient amplitude; f = oscillation frequency; t_{ramp} = gradient ramp-up time from zero gradient to the maximum gradient value; δ = diffusion gradient pulse duration; Δ = diffusion gradient separation. MPG, motion probing gradient; OGSE, oscillating-gradient spin-echo; PGSE, pulsed-gradient spin-echo.

[Δ] = 47.3 ms; δ = 36.3 ms). When the TE of the PGSE DWI sequence was set to be the same as that of the OGSE DWI sequence, the Δ_{eff} value of the PGSE sequence was 35.2 ms. For the OGSE DWI sequence, the b-value is given by

$$b = 2N\gamma^2 M_{enc}{}^2 \Delta_{\text{eff}} = 2N\gamma^2 G^2 \left(\frac{1}{4f} - \frac{t_{ramp}}{2}\right)^2 \Delta_{\text{eff}}$$

where N denotes the total number of oscillation cycles, γ represents the hydrogen nuclear gyromagnetic ratio, M_{enc} denotes the 0th moment of the first lobe of the oscillating diffusion-encoding gradients, G is the maximum gradient amplitude, f is the oscillation frequency, and t_{ramp} is the gradient ramp-up time from zero gradient to the maximum gradient value (Fig. 1). The Δ_{eff} was defined by comparison with the b-value calculation for the PGSE DWI sequence. Parameters of the OGSE DWI sequence were as follows: N = 2; G = 96.7 mT/m; f = 30 Hz; and t_{ramp} = 1.5 ms. For the PGSE acquisition with N = 1, Δ_{eff} reverts to $\Delta - \delta/3$. The parameter of the PGSE DWI sequence was as follows: G = 17.4 mT/m. Other OGSE and PGSE sequence parameters were as follows: TR, 4800 ms; TE, 101 ms; FOV, 200 × 200 mm^2; matrix size, 82 × 82; slice thickness, 5 mm; and acquisition time, approximately 2 mins. ROIs were placed within the brain abscesses, surrounding hyperintensity lesions on T2-weighted image, and normal white matter contralateral to each brain abscess on DTI eigenvalues (λ1, λ2, and λ3) maps and mean diffusivity (MD) maps. For normal white matter, three circular ROIs of 330 mm^3 were placed, and the averages of the values were calculated. The relative percentage change between shorter and longer diffusion times was then calculated as:

$$\left(Value_{\Delta eff=6.5ms} - Value_{\Delta eff=35.2ms}\right)/Value_{\Delta eff=35.2ms} \times 100\ (\%)$$

where $Value_{\Delta eff}$ is λ1, λ2, λ3, or MD obtained using the OGSE and PGSE sequences, respectively.

Figures 2 and 3 show the DWIs, λ1, λ2, λ3, and MD maps of patient 1, and Fig. 4 shows those of patient 2. The contrast-enhanced T1-weighted images showed ring enhancement, and DWIs showed a marked internal high signal (arrows), which are typical images of brain abscesses. The brain abscesses (arrows) showed high intensity on DWI with a Δ_{eff} of 35.2 ms. On the other hand, the lesions showed decreased visualization on DWI with a Δ_{eff} value of 6.5 ms. Fig. 5 shows the λ1, λ2, λ3, and MD values and the relative percentage change between shorter and longer diffusion times for each brain abscess, surrounding hyperintensity lesions on T2-weighted image, and normal white matter contralateral to each brain abscess. The λ1, λ2, λ3, and MD values of all lesions appear higher at short Δ_{eff} values than at long Δ_{eff} values. The relative percentage change is highest for brain abscesses rather than surrounding hyperintensity lesions and normal white matter.

So far, it has been assumed that the markedly high signal on DWI of abscesses is due to increased viscosity. If the high signal on DWI of brain abscesses is due to the viscosity of an isotropic medium, the diffusion coefficient should not change even if the diffusion time is changed. However, the lesions showed a marked diffusion-time dependence of λ1, λ2, λ3, and MD within a Δ_{eff} range of 6.5–35.2 ms used in

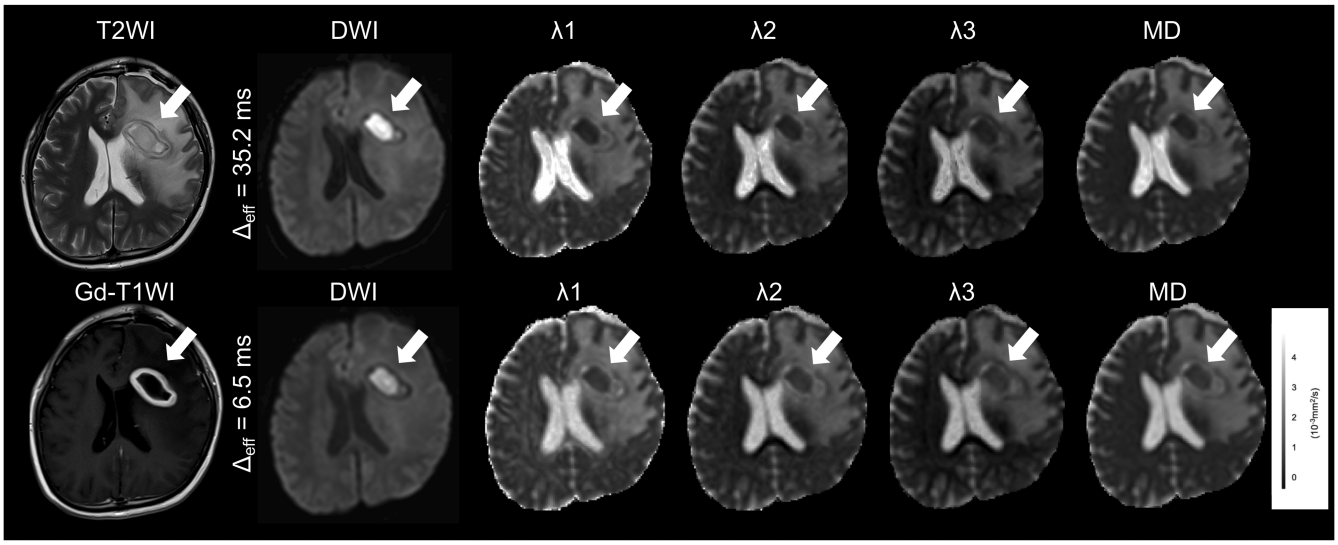

Fig. 2 T2WI; Gd-T1WI; DWI; and diffusion eigenvalue λ1, λ2, λ3, and MD maps with an Δ_{eff} of 35.2 ms and 6.5 ms of brain abscess I (arrows) from patient 1. The brain abscess showed high intensity on DWI with an Δ_{eff} of 35.2 ms and decreased visualization on DWI with an Δ_{eff} of 6.5 ms. λ1, λ2, λ3, and MD of brain abscess showed higher at the Δ_{eff} of 6.5 ms, compared with those at the Δ_{eff} of 35.2 ms. Δ_{eff}, effective diffusion time; DWI, diffusion-weighted images; Gd-T1WI, gadolinium contrast-enhanced T1-weighted images; MD, mean diffusivity; T2WI, T2-weighted image.

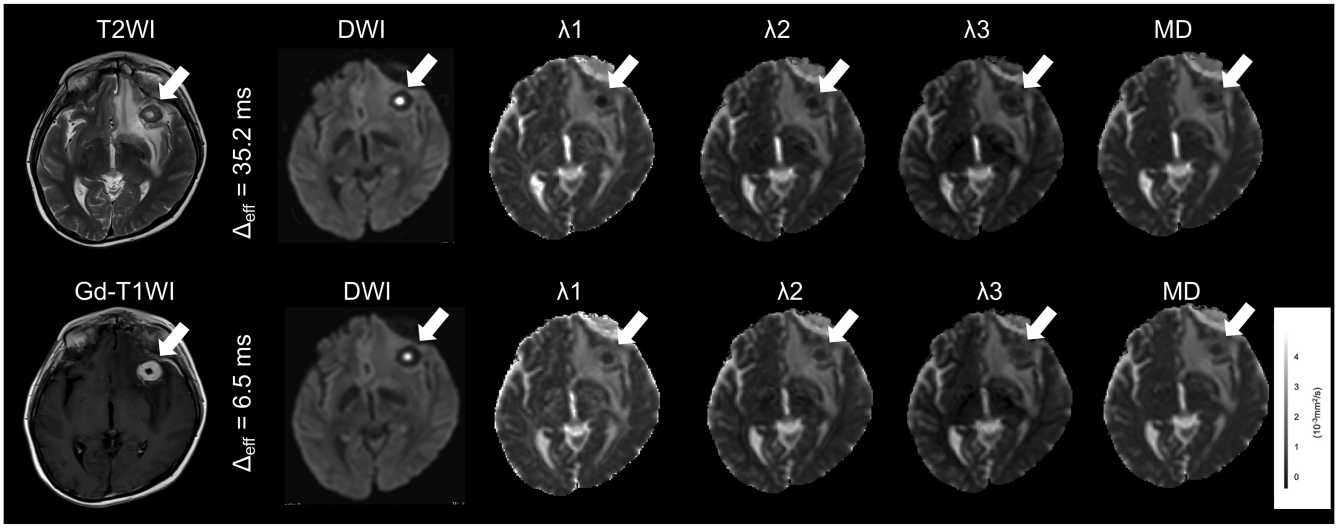

Fig. 3 T2WI; Gd-T1WI; DWI; and diffusion eigenvalue λ1, λ2, λ3, and MD maps with an Δ_{eff} of 35.2 ms and 6.5 ms of brain abscess II (arrows) from patient 1. The brain abscess showed high intensity on DWI with an Δ_{eff} of 35.2 ms and decreased visualization on DWI with an Δ_{eff} of 6.5 ms. λ1, λ2, λ3, and MD of brain abscess showed higher at the Δ_{eff} of 6.5 ms, compared with those at the Δ_{eff} of 35.2 ms. Δ_{eff}, effective diffusion time; DWI, diffusion-weighted images; Gd-T1WI, gadolinium contrast-enhanced T1-weighted images; MD, mean diffusivity; T2WI, T2-weighted image.

this study. This diffusion-time dependence suggests spatially restricted diffusion.

The abscess begins as a localized host acute inflammatory response to infection. The center of the abscess contains an acute inflammatory exudate composed of inflammatory cells, necrotic tissue debris, fibrin, and bacteria.[12] Maturation of the abscess involves fibroblastic proliferation and tissue repair at the abscess boundary, and formation of a fibrous capsule at the periphery. The mean square displacements of water molecule movement for Δ_{eff} of 6.5 ms and 35.2 ms are 11 μm and 25 μm, respectively, for free diffusion at the patient's body temperature by the Einstein-Smoluchowski equation. Our results suggest that abscesses contain microstructures, such as inflammatory cells, necrotic tissue debris, fibrin, and bacteria, with hindered diffusion at mean square displacements of 11–25 μm (Fig. 6). Abscess III shows anisotropic diffusion compared to abscess I

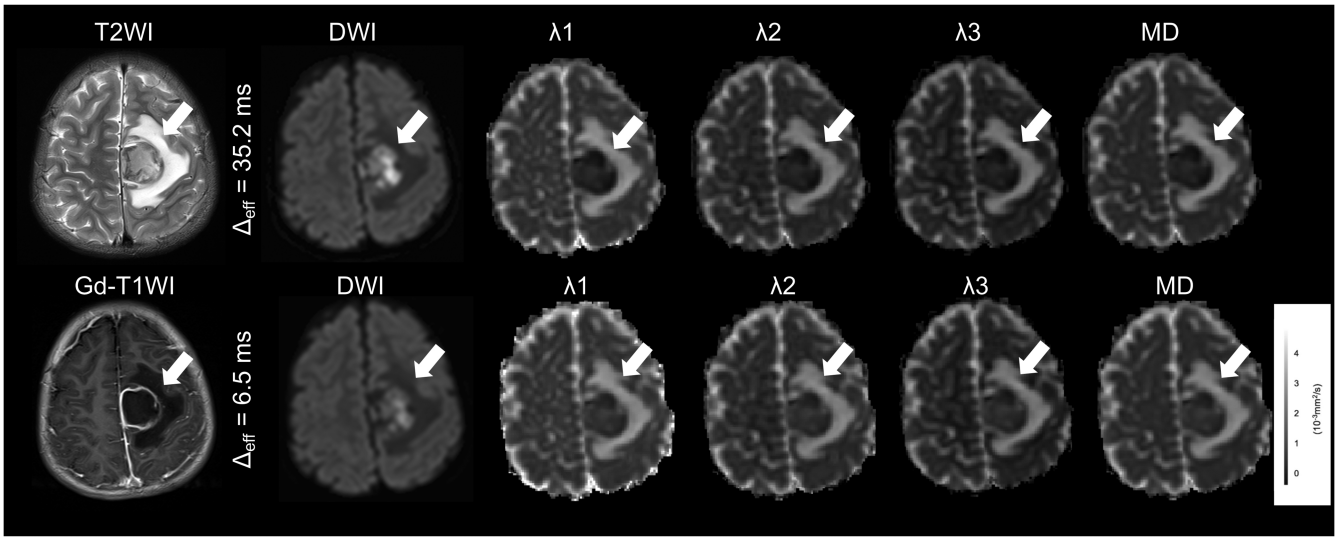

Fig. 4 T2WI; Gd-T1WI; DWI; and diffusion eigenvalue λ1, λ2, λ3, and MD maps with an Δ_{eff} of 35.2 ms and 6.5 ms of brain abscess III (arrows) from patient 2. The brain abscess showed high intensity on DWI with an Δ_{eff} of 35.2 ms and decreased visualization on DWI with an Δ_{eff} of 6.5 ms. λ1, λ2, λ3, and MD of brain abscess showed higher at the Δ_{eff} of 6.5 ms, compared with those at the Δ_{eff} of 35.2 ms. Δ_{eff}, effective diffusion time; DWI, diffusion-weighted images; Gd-T1WI, gadolinium contrast-enhanced T1-weighted images; MD, mean diffusivity; T2WI, T2-weighted image.

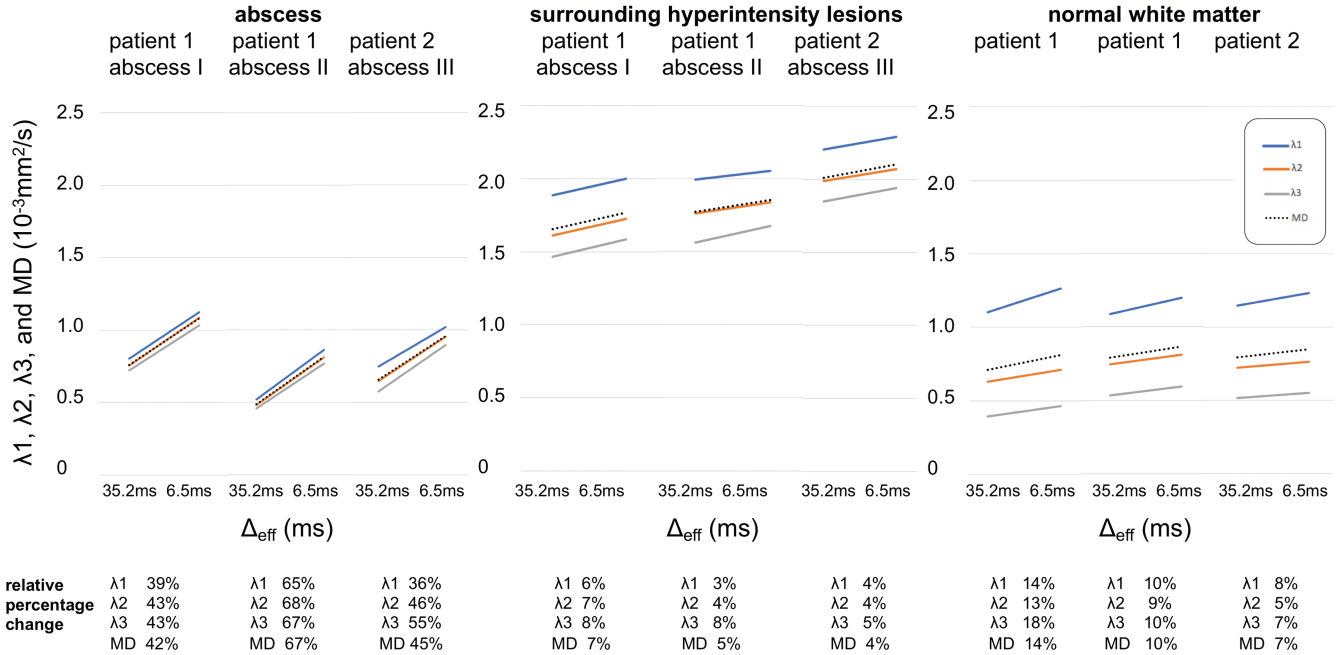

Fig. 5 The diffusion eigenvalue λ1, λ2, λ3, and MD values and the relative percentage change between shorter and longer diffusion times for each brain abscess, surrounding hyperintensity lesions on T2-weighted image, and normal white matter contralateral to each brain abscess. The λ1, λ2, λ3, and MD values of all lesions appear higher at short Δ_{eff} as compared to those at long Δ_{eff} values. Δ_{eff}, effective diffusion time; MD, mean diffusivity.

and II, and directional dependence was also observed in the relative percentage change. Presumably, abscesses I and II may have contained a higher percentage of exudate with less anisotropic diffusion, while abscess III may have contained a higher percentage of contents with anisotropic diffusions, such as necrotic tissue debris and fibrin. If we could perform investigations with Δ_{eff} values smaller than 6.5 ms and eliminate the influence of spatially restricted diffusion, we could confirm the intrinsic diffusion coefficient values due to the viscosity of the abscess, and separate diffusion coefficient contributions from substrate viscosity and spatially restricted diffusion in lesions.

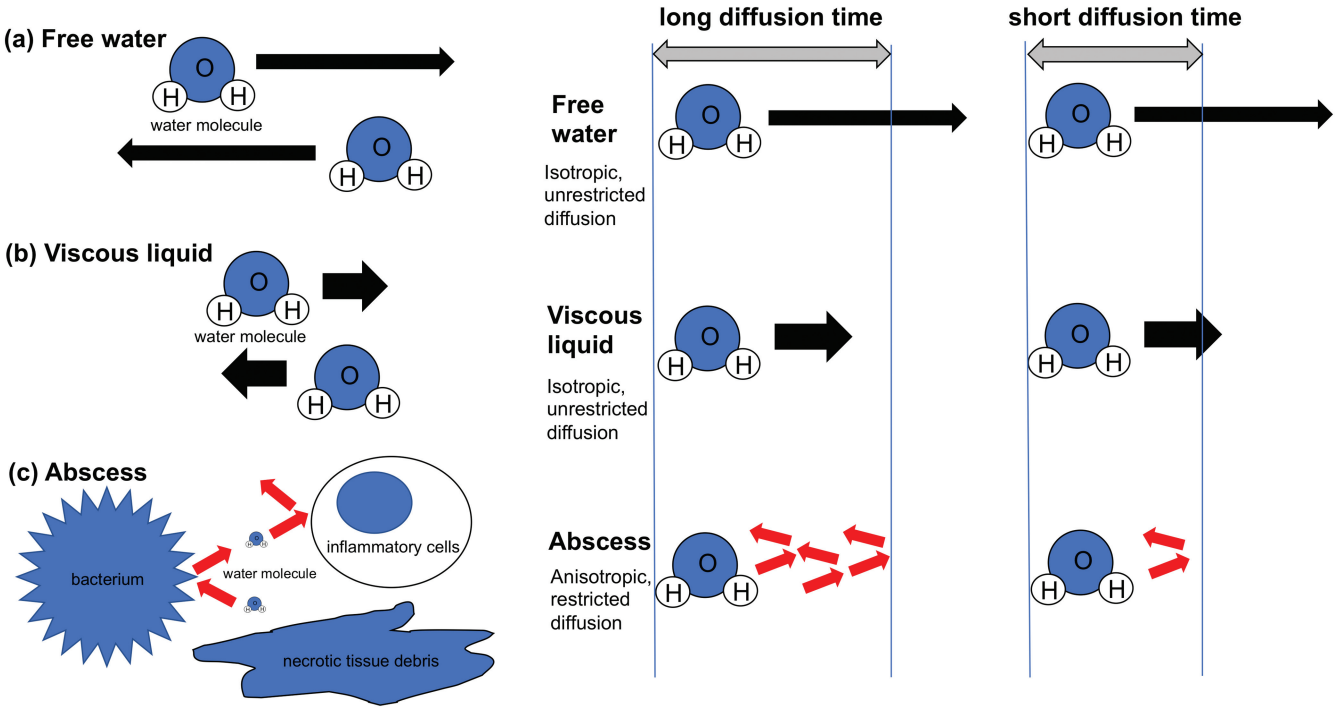

Fig. 6 (**a**) In free water of isotropic diffusion, water molecules can be free to move around. If most molecules do not move far enough to interact with any obstacle during the preset diffusion time, the diffusion coefficient is the intrinsic diffusion coefficient of cellular water. (**b**) Within a viscous liquid of isotropic diffusion, the rate of movement of water molecules decreases rather than free water. Since there is no obstacle, the diffusion coefficient of viscous liquid does not change even if the diffusion time is changed. (**c**) In addition to the slow movement of water molecules from viscosity, the rate of movement is probably restricted by inflammatory cells, bacterium, necrotic tissue debris, and other internal structures in abscesses. As the diffusion time increases, molecules interact with more barriers, and the observed diffusion coefficient decreases asymptotically.

A previous study reported a time dependence of diffusion coefficients in the normal white matter with decreasing ADC for increasing diffusion times. Besides, the rise in ADC in response to a decrease in the diffusion time is a key feature to extract the cell size. The range of axon sizes in white matter is 1–6 μm, which is smaller than the microstructure in brain abscesses. Therefore, the spatial restriction of diffusion in white matter is stronger than that in brain abscesses, and the relative percentage change in diffusion time between 6.5 ms and 35.2 ms is lower in white matter than in brain abscesses. Moreover, the surrounding hyperintensity lesions reflect cerebral edema and inflammation. In cerebral edema and inflammation, the diffusion coefficient increases with excessive water accumulated in the intracellular and extracellular spaces. The spatial restriction of diffusion in cerebral edema and inflammation is stronger than in normal white matter due to axonal swelling, and the relative percentage change in diffusion time between 6.5 ms and 35.2 ms is slightly lower in cerebral edema and inflammation than in normal white matter.

In conclusion, the markedly high signal on DWI of abscesses is not only due to substrate viscosity but also due to restricted diffusion caused by the microstructure within the lesions.

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Conflicts of Interest

Katsutoshi Murata is an employee of Siemens Healthcare K. K., Japan. Thorsten Feiweier is an employee of Siemens Healthcare GmbH, Germany. Thorsten Feiweier has stock ownership Siemens (Healthineers) AG. Osamu Abe receives a lecture fee from Siemens Healthcare KK and has a grant from Siemens Healthcare KK. All remaining authors declare no potential conflicts of interest associated with this work.

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