EFFECT OF CELL MEMBRANE WATER PERMEABILITY ON DIFFUSION-WEIGHTED MR SIGNAL: A STUDY USING EXPRESSION-CONTROLLED AQUAPORIN4 CELLS

Takayuki Obata[1], Jeff Kershaw[2], Daigo Kuroiwa[1], Sayaka Shibata[2], Abe Yoichiro[3], Masato Yasui[3], and Ichio Aoki[2]

[1]Center for Charged Particle Therapy, National Institute of Radiological Sciences (NIRS), Chiba, Chiba, Japan, [2]Molecular Imaging Center, NIRS, [3]Department of Pharmacology, Keio University, Tokyo, Japan

INTRODUCTION

Diffusion-weighted magnetic resonance imaging (DWI) plays an important role in diagnosing diseases such as brain infarction and cancer. Although it is understood that signal attenuation is due to the diffusion of water molecules, a reliable quantitative signal model relating tissue parameters and signal contrast remains to be established. Cell membrane water permeability (CMP) is one factor that may affect DWI signal contrast. Aquaporin4 (AQP4) is a channel located in the cell membrane that is known to facilitate water exchange and therefore affect CMP and perhaps DWI contrast. In this study, we performed multi-b-value and multi-diffusion-time DWI on AQP4-nonexpressed (noAQ) and AQP4-expressed (AQ) cells to investigate the effect that CMP has on diffusion-weighted magnetic resonance signal.

METHODS

A 7T animal MRI (Kobelco and Bruker, Japan) system was used for this experiment. Two types of cells (noAQ and AQ) suspended in PBS were set in the gantry.

Multi b-value DWI was obtained using a pulsed-gradient spin-echo (PGSE) sequence (TR = 3s and TE = 90 ms). The b-value was increased from 0 to 8000 s/mm^2 in 14 steps by increasing the gradient amplitude (Δ=25ms, δ=7ms). Under the assumption that the signal (S(b)) includes two compartments (fast (FD) and slow diffusion (SD)), biexponential curve fitting was performed with respect to b-value with S(b)=S0*(Ff*exp(-Df*b) + Fs*exp(-Ds*b)), where Df, Ds are the compartmental diffusion coefficients, and Ff and Fs (Ff+Fs=1) are the compartmental volume fractions.

Multi-diffusion-time DWI was obtained using an oscillating-gradient spin-echo (OGSE) sequence (Does2003, Parsons2003). Images were acquired with b-values of 0 & 405 s/mm^2 and effective diffusion-times of 0.96, 1.2, 2.4, 4.8 and 9.6 ms.

RESULTS

Single-exponential fitting to the images in the range b=0-1500 indicated that both the noAQ and AQ samples had depth-dependent ADC changes, which may reflect depth-dependent extra-cellular space changes (Fig1, left). Single-exponential fitting to the b=3000-8000 images found a clear difference between the ADCs of the noAQ and AQ samples (Fig 1, right). After biexponential fitting across the full b-value range, the only parameter to show a significant difference between the noAQ and AQ cells was Ds (Fig 2). From the OGSE data, similar diffusion-time dependent ADC changes were observed in both the noAQ and AQ cells (Fig 3), meaning that the dominant restriction effects are similar in both cell types.

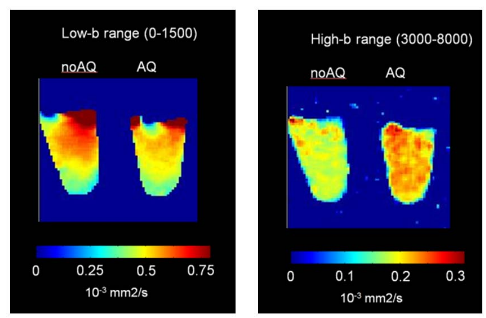

Fig 1. ADC maps of noAQ and AQ calculated using a low (left) and high (right) ranges of b-values. Both noAQ and AQ have depth-dependent ADC changes in the low-b range, and there is a clear difference between the ADCs of the noAQ and AQ in the high-b range.

DISCUSSION and CONCLUSION

The absence of a significant difference in Df for the AQ and noAQ suggests that CMP does not affect extracellular water diffusion. The OGSE results are consistent with this because the max b-value was only 405 s/mm^2, which is in the range where the signal is still dominated by the FD contribution. The significant difference in Ds may indicate that the SD water molecules are more restricted by the lower CMP of the noAQ cells.

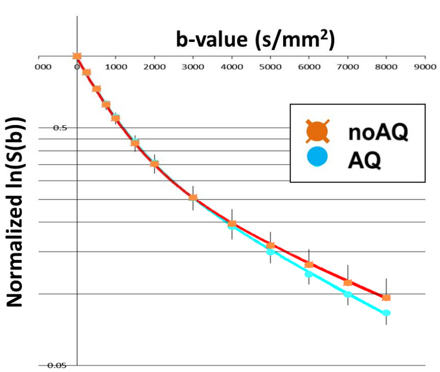

Fig 2. b-value dependent signal changes (mean ±SD) and bi-exponential fitting curves. The curves are similar in the range b = 0-1500, but differ at higher b-values.

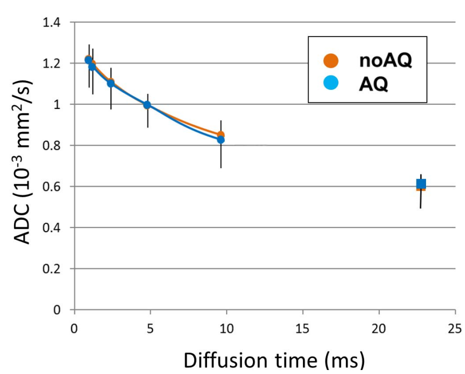

Fig 3. Diffusion-time dependent ADC changes (mean±SD) calculated from OGSE (circles). ADCs from PGSE data (b=0-500) are also shown for reference (rectangles).