Apparent exchange rate of water in human brain matter revealed by a novel pulse sequence

M. Nilsson1, D. Topgaard2, S. Brockstedt3, F. Ståhlberg4, and J. Lätt1,5
1Department of Medical Radiation Physics, Lund University, Lund, Sweden, 2Physical Chemistry, Lund University, Lund, Sweden, 3Department of Diagnostic Radiology, Lund University, Lund, Sweden, 4Center for Medical Imaging and Physiology, Lund University Hospital, Lund, Sweden

Introduction
Diffusion MRI using pulsed gradient spin echoes (PGSE) is known to yield information about tissue microstructure; for instance, measurements with different diffusion times (TD) provide structural information regarding cellular size distributions [1]. Recent studies have shown that exchange may affect PGSE measurements in white matter [2] and in sub-acute stroke lesions [3]. However, cell membrane permeability, i.e. the water exchange rate, is seldom estimated due to the limited sensitivity of the PGSE sequence. A sequence more sensitive to exchange than the PGSE sequence would be desirable to probe the cell membrane permeability, which is expected to be altered for several types of brain pathology [4]. In this study, we employed a novel pulse sequence at an MRI scanner, previously implemented at an NMR spectrometer [5], to measure the apparent water exchange rate in both a phantom and in vivo.

Theory
A schematic overview of the sequence is presented in Fig. 1. A diffusion weighted (DW) block precede an ordinary DWI sequence, which selectively attenuate the signal from the fast diffusion component. The diffusion sensitivity from the first pair of gradients is denoted by and from the second pair is denoted by , with and . To estimate the apparent exchange rate (AXR), the apparent diffusion coefficient (ADC) was measured using two different -values in the DWI-block while varying the mixing time (TM) and applying a fixed . The equilibrium ADCeq was estimated using a short TM (approximately 20 ms) and . Analysis was performed using the following equation

\[ S = A \exp (-b \cdot ADC_f) \]

where \( A \) is the signal strength for \( b = 0 \), ADCf is the ADC after filtering and \( \sigma \) is the filter size, set to zero when \( b = 0 \) and limited to a maximal value of unity. In a two component system with two distinct ADCs, \( \text{AXR} = (1 + f_1 f_2 / f_1) k_1 \) where \( f_1 \) and \( f_2 \) are the volume fractions of the slow and fast diffusion components and \( k_1 \) is the exchange rate of the slow diffusion component.

Method
Measurements were performed at an Philips 3TAchieva system in a phantom of baker’s yeast at room temperature as well as in healthy volunteers. Informed consent was obtained. The in vivo measurements were performed with: TE/TR = 97/2500 ms, and . Temperature as well as in healthy volunteers. Informed consent was obtained. The sequence is sensitive to exchange between water pools with different diffusion coefficients. The results from yeast phantom measurements agreed with previous NMR spectrometry studies [5]. In vivo results showed effects of exchange in brain matter. One potential error source is compartmentally different T1-relaxation times, although it is likely of minor influence in vivo [6]. Assuming \( f_1 = f_2 \), the exchange rate \( k_1 \) were in the order of \( 1 \text{s}^{-1} \), values which would have been inaccessible using a PGSE or PGSTE sequence with varied TD. The estimated AXR is the most noise-sensitive of the estimated parameters and it is not expected to be sensitive to the measurement direction. The signal-to-noise ratio in the deep parts of the brain was approximately half as compared to outer parts of the brain, which might affect the estimated AXR in the central brain.

In conclusion, the apparent exchange rate can be estimated in vivo using this novel pulse sequence. This is potentially a very useful contrast mechanism in MRI.

References

Fig. 1. Illustration of the pulse sequence employed for permeability-sensitive diffusion MRI. A filtering DW block and an adjustable delay of duration TM precede a standard DWI sequence. Each DW block contains a pair of diffusion sensitizing gradient pulses of duration and amplitude . The time between the onset of the pulses in the pulse pair is denoted . The filtering block is designed to selectively attenuate the signal from the fast diffusion component.

Fig. 2 (above). Parametric maps of \( \text{ADC}_{\text{eq}} \), \( \sigma \) and AXR. The \( \text{ADC}_{\text{eq}} \) decreases slightly from top to bottom due to sedimentation. Rightmost: \( \text{ADC} \) estimated for each TM shown by crosses and model fit as a solid line, with data obtained from the ROI shown in red in the \( \text{ADC}_{\text{eq}} \) map.

Fig. 3 (right). Top row: Parametric maps of \( \text{ADC}_{\text{eq}} \), \( \sigma \) and AXR. Areas with \( \text{ADC}_{\text{eq}} \) greater than 1.2 \( \mu \text{m}^2/\text{ms} \) were marked with blue in the \( \sigma \) and AXR map. Extreme values in the AXR and \( \sigma \) maps, identified by unsuccessful model fits, were replaced by the median of their neighbours. The observed AXR was mainly in the range between 1 and 2.5 \( \text{s}^{-1} \). Bottom row: The crosses shows that \( \text{AXR} \) increases with TM, indicating exchange, with data obtained from ROIs shown in green in the \( \text{ADC}_{\text{eq}} \) map. Model fit is shown as a solid line and the observed AXR-values were 1.5, 0.5 and 1.6 \( \text{s}^{-1} \).

Discussion and conclusion
A pulse sequence, originally developed for studying cell membrane permeability using an NMR spectrometer [5], was successfully implemented at a clinical MRI scanner. The sequence is sensitive to exchange between water pools with different diffusion coefficients. The results from yeast phantom measurements agreed with previous NMR spectrometry studies [5]. In vivo results showed effects of exchange in brain matter. One potential error source is compartmentally different T1-relaxation times, although it is likely of minor influence in vivo [6]. Assuming \( f_1 = f_2 \), the exchange rate \( k_1 \) were in the order of \( 1 \text{s}^{-1} \), values which would have been inaccessible using a PGSE or PGSTE sequence with varied TD. The estimated AXR is the most noise-sensitive of the estimated parameters and it is not expected to be sensitive to the measurement direction. The signal-to-noise ratio in the deep parts of the brain was approximately half as compared to outer parts of the brain, which might affect the estimated AXR in the central brain.

In conclusion, the apparent exchange rate can be estimated in vivo using this novel pulse sequence. This is potentially a very useful contrast mechanism in MRI.