How to suppress the contribution from pseudo-diffusion in oscillating gradient diffusion MRI

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Target audience: Investigators who are interested in oscillating gradient diffusion MRI on clinical scanners.

Purpose: Oscillating gradient spin-echo (OGSE) diffusion MRI has recently drawn attentions due to its unique ability to distinguish tissue microstructures at varying length scales [1-2]. Applications of this technique, however, remained limited due to the relatively low diffusion weighting, or b-value ($b \propto 1/f^3$), available on current clinical [3-4] and preclinical [5] scanners. It is known that conventional pulsed gradient spin echo (PGSE) diffusion measurements at low b values contain contributions from perfusion related pseudo-diffusion [6-7]. Here, we examined the effects of pseudo-diffusion on OGSE signals at low-b-values, and developed a new sequence that combined orthogonal pulsed and oscillating gradients to suppress the contributions from pseudo-diffusion.

Methods: When the pulsed and oscillating gradients are placed on orthogonal directions, the hybrid gradient waveform can be expressed as a complex number (g = g1+i*g2) (Fig. 1). The temporal diffusion spectrum of the hybrid gradient $F(\omega) = \int\int_0^t g(\tau)d\tau \cdot e^{-i\omega t}dt$ is a linear combination of the spectra of the individual gradients (Fig. 1). The b-value of the hybrid gradient waveform can be calculated based on the complex representation:

$$b = \gamma^2 \int \left[\int_0^t g_1(\tau) + i * g_2(t)d\tau\right] * \left[\int_0^t g_1(\tau) - i * g_2(t)d\tau\right] dt$$

$$= \gamma^2 \int \left[\int_0^t g_1(\tau)d\tau\right]^2 dt + \gamma^2 \int \left[\int_0^t g_2(\tau)d\tau\right]^2 dt - i * \gamma^2 \int \left[2\int_0^t g_1(\tau)d\tau \cdot \int_0^t g_2(\tau)d\tau\right] dt$$

where the third term (imaginary part) does not contribute to the diffusion attenuation, and therefore, b-values from the two orthogonal gradients are linearly addable. The apparent diffusion coefficient (ADC) is calculated as $\mathrm{ADC(OGSE^*)} = -\frac{1}{b_{hybrid} - b_{PGSE}} \log\left|\frac{S_{hybrid}}{S_{PGSE}}\right|$. In this way, the addition of the pulsed gradient will not affect the sensitivity of the sequence to time dependent diffusion. In vivo tests were performed on normal adult mice (n=5) on an 11.7 T horizontal NMR spectrometer (maximum gradient strength = 760 mT/m) with a dual channel cryongenic transmit-receiver coil. The hybrid sequence with pulsed gradients ([0 0 1; 1 0 0; 0 1 0; 0 0 1; 1 0 0; 0 1 0], b = 300 s/mm^2) and orthogonal cosine-trapezoid oscillating gradient ([1 1 0; 0 1 1; 1 0 1; 1 -1 0; 0 1 -1; -1 0 1], b = 50-600 s/mm^2 for 100Hz and 50-300 s/mm^2 for 200Hz) were acquired: TE/TR = 32/1500 ms, four-segment EPI readout, one average, four repetitions, resolution = 0.2 mm x 0.2 mm x 1 mm. The pseudo-diffusion suppressed ADC (OGSE*) values were averaged over six directions. For comparison, OGSE-only and PGSE-only (δ/Δ = 10/13.2 ms, b = 50-1000 s/mm^2) diffusion data were acquired using the same parameters, and b-values from all experiments were calibrated using a gel phantom placed beside the mouse brain.

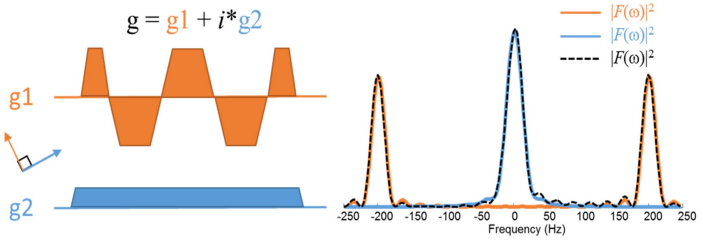

Fig. 1 Diagram of the hybrid diffusion sequence with the oscillating gradient (g1) and pulsed gradient (g2) on orthogonal directions. The spectrum of the gradient waveform is a linear combination of the spectra of g1 and g2.

Results: We focused on the mouse cortex in this study, which has the highest SNR (68±8 in single repetition b_0 images, n=5) and relatively homogenous microstructures (ROI defined in Fig. 2 inset). Pseudo-diffusion was observed in both PGSE and OGSE measurements, characterized by significantly increased ADC values at low b-values (e.g., 50 s/mm^2) compared to those at high b-values (>300 s/mm^2) (solid lines in Fig. 2A). As a result, ADC measured at b≤200 s/mm^2 (when pseudo-diffusion is present) from different oscillating frequency showed no significant difference (p≥0.05, 1-way ANOVA, n=5). With the hybrid pulsed and oscillating gradient sequence, the contribution from pseudo-diffusion was significantly reduced (p<0.01 for b=50-100 s/mm^2, dashed lines in Fig. 2B) and the derived ADC-values remained relatively unchanged with increasing b values (150-700 s/mm^2). At b≥300s/mm^2, the OGSE* and the OGSE-only curves converged at the same ADC values, suggesting that the pseudo-diffusion component in the OGSE* measurements was mostly suppressed.

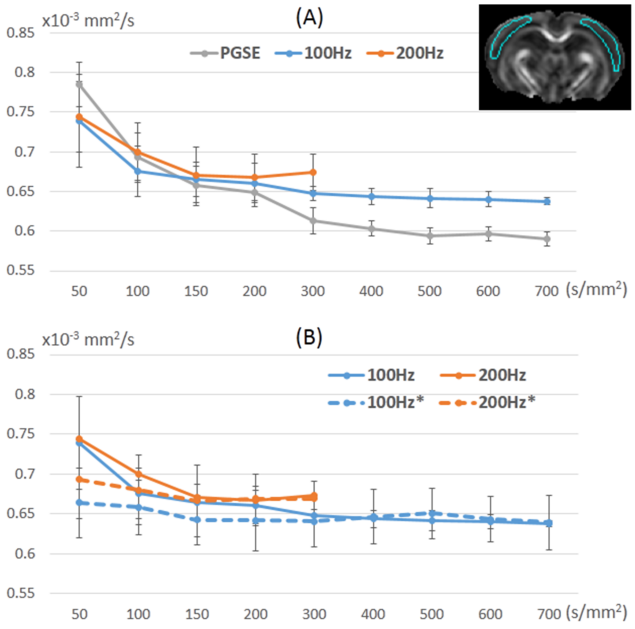

Fig. 2 (A) PGSE and OGSE measurements at b = 50-700 s/mm^2 (n=5). (B) Pseudo-diffusion suppressed ADC (100Hz* and 200Hz*, dashed lines) obtained using the hybrid sequence, compared with measurements from (A) (solid lines).

Discussions and conclusions: We demonstrated that OGSE diffusion MRI was also sensitive to pseudo-diffusion, which reduced the sensitivity to time dependent diffusion. The contributions from pseudo-diffusion could be suppressed using the proposed hybrid pulsed and oscillating gradient sequence. The results suggest that the hybrid sequence can provide a practical solution for future applications of OGSE diffusion MRI on clinical scanners.

References: 1) MRM 2003 49(2):206-15. 2) NMR Biomed 2010 23(7):745-56. 3) MRM 2014 71(1):83-94. 4) MRM 2014 72(3):726-39. 5) MRM 2014 72(3):726-39. 6) Radiology 1988 168(2):-505. 7) Radiology 2008 249(3):548-52.