# Apparent Diffusion Coefficient Pattern Under Different Diffusion Times in OGSE

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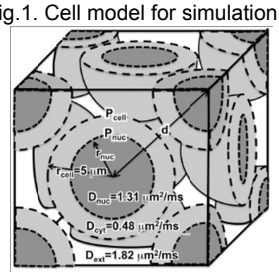
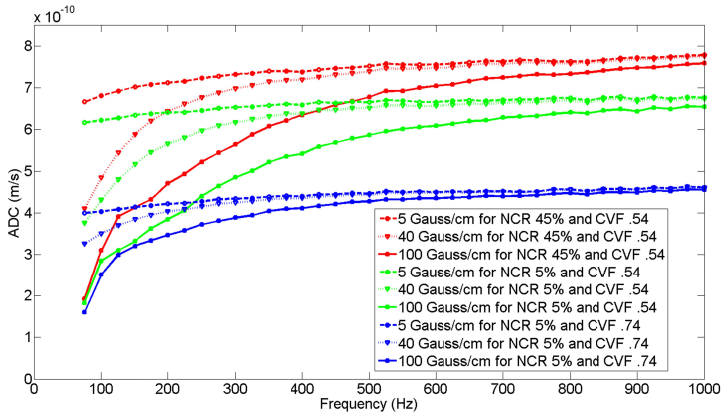
Introduction: There has been much recent research into the use of diffusion weighted magnetic resonance imaging (DWI) to provide information on tissue structure. The pulse gradient spin echo (PGSE) sequence for DWI [1] offers a way to measure the rate of the diffusion, known as the apparent diffusion coefficient (ADC), on a timescale, Δ, equal to the separation between pulses. Gradient hardware considerations limit conventional PGSE's to probing fairly long diffusion times, normally > 10ms, limiting the information available about underlying tissue structure. Oscillating gradient spin echo (OGSE) sequences [2], on the other hand, sample diffusion times of 3/(8*f), where f is the frequency of oscillation, allowing a range of diffusion times down to ~1 ms to be probed. Thus, OGSE can potentially provide more detailed information about tissue microstructure. In this research, we use a Monte Carlo simulation of DWI using OGSE in a tissue model to relate the diffusion time-dependent behaviour of the ADC to details of the tissue microstructure. We then experimentally validate our simulation results on a 3T clinical scanner and compare results to a standard PGSE.

Fig.1. Cell model for simulation




Methods & Analysis: We use an idealized complex tissue model with semi permeable membranes, shown by Figure 1 [3], for the Monte Carlo simulation [4]. In this study we simulate microstructural differences by changing the NCR (nucleus to cell volume ratio), through changes in the nuclear radius, $r_{nuc}$, and the CVF (cell volume fraction), through changes in the distance between cell centres. We simulate oscillating diffusion gradients with amplitudes 5 Gauss/cm, 40 Gauss/cm and 100 Gauss/cm with oscillation frequencies ranging from 50Hz to 1000Hz in 25Hz increments. At each gradient amplitude and frequency, signals at two *b*-values are obtained and the ADC is calculated using the well known relationship, $S=S_0\exp(-b*ADC)$ [Eq 1], where $S_o$ is the signal in the absence of a diffusion gradient. In our experiments, we use fresh chicken thigh, as the scanning sample. Diffusion in this sample is expected to be generally isotropic, given the various orientations of muscle fibre over the entire sample. Scans are performed on a GE MR750 3.0T with a maximum gradient strength of 5 Gauss/cm. For PGSE experiments, we use a built-in PGSE sequence to obtain five equally spaced *b*-values from 200 to 1000 s/mm$^2$. The built-in sequence is such that diffusion time is not under our control, and the associated diffusion times for these *b*-values are 11ms, 14ms, 16ms, 18ms and 19ms, respectively. ADC for each diffusion time is then estimated using [Eq 1] with a single *b*-value and assuming a mono-exponential fit. Implementation of a custom OGSE sequence on the MR750 was performed. Equally spaced frequencies from 50Hz to 225Hz at the maximum gradient amplitude of 5 Gauss/cm are investigated, and for each frequency, the ADC is estimated using the signal at two different *b*-values (similar to Monte Carlo analysis). Sixteen times averaging of experimental data is used to improve the signal to noise ratio prior to analysis.

Fig.2. Simulated ADC pattern at multiple model structures




Results: Fig 2 shows the results of the Monte Carlo simulations. Each colour represents a different NCR/CVF microstructure. An expected ADC pattern is observed, where at shorter diffusion times (higher frequencies), ADC increases. At high frequencies, the ADC's at all gradient strengths converge to a single free diffusion coefficient that is different for each microstructure. With increasing NCR, the free diffusion coefficient becomes greater due to faster diffusion in the nucleus than in the cytoplasm, while increasing CVF decreases the free diffusion coefficient because of decreased contribution from the fast-diffusing extracellular fluid. We also note that at long diffusion time (f=75Hz, diffusion time=5ms) the ADC's at 100 Gauss/cm for all microstructures become almost identical, implying a loss of information about the microstructure. Finally, Fig 2 shows that higher than clinical gradient strengths may be required to see significant variations in ADC with diffusion time (gradient frequency). Fig 3 shows the results of the OGSE experiments in chicken thigh. At each OGSE frequency, the corresponding diffusion time is shown. The behaviour of ADC with OGSE frequency is qualitatively similar to that observed in the Monte Carlo simulations, indicating the effects of tissue microstructure possibly related to NCR and CVF. Experimental PGSE results in Fig 4, on the other hand, show little variation in ADC with diffusion time. Possible explanations are the loss of all microstructural information at the long (min. 11 ms) diffusion times sampled and also inaccuracies inherent in estimating ADC from a single *b*-value.

Fig.3. OGSE ADC pattern

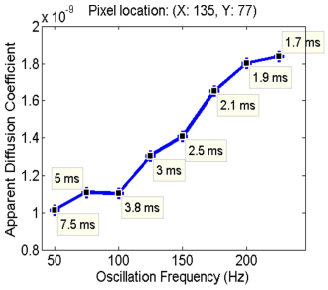
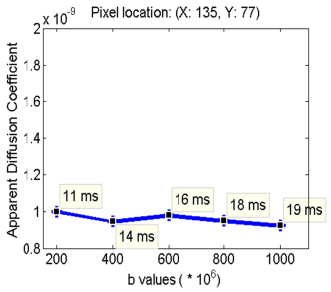



Fig.4. PGSE ADC pattern




Conclusion and Future Work: **1.** Using a Monte Carlo simulation, we have analyzed the behaviour of ADC with diffusion time for different tissue microstructures (NCR and CVF). As far as we are aware, this is the first description on ADC pattern based on different NCR and CVF. The study suggests that OGSE's, with their ability to sample short diffusion times, have the potential to provide information about the microstructure of scanned biological tissue. Specifically, the ADC at high frequencies (short diffusion times), representing the free diffusion coefficient, may be representative of a given microstructure. **2.** Experiments at 5 Gauss/cm, which is much lower than ever previously reported in diffusion experiment, qualitatively confirm the behaviour of ADC with diffusion time at lower OGSE frequencies (frequencies above 225 Hz are currently unavailable experimentally), while PGSE experiments show little variation of ADC with diffusion time, possibly owing to the long diffusion times sampled (min. 11 ms). **3.** Simulations indicate that higher gradient strengths are preferable for probing ADC behaviour when using OGSE. **4.** A quantitative analysis on the ADC pattern in OGSE experiments is currently being pursued to gain more valuable insight into the microstructural information available.

References: **1.** P. T. Callaghan, J Mag Res **129,** 74–84 (1997); **2.** Xu J, Does MG, Gore JC. Mag Res Med 61:828-833 (2009); **3.** Hall MG, Alexander DC. IEEE Trans Med Imag 28:1354-1364 (2009); **4.** B. Walters and J. K. Kim, *A Monte Carlo Study of DWI Contrast…Using OGSE*, submitted to J Mag Res on September 23, 2011