

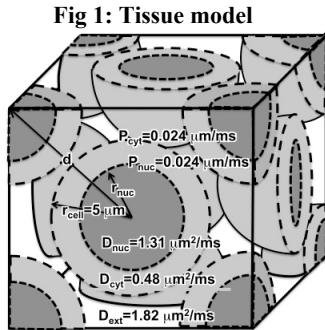
DWI Contrast between Healthy and Malignant Tissue using OGSE's

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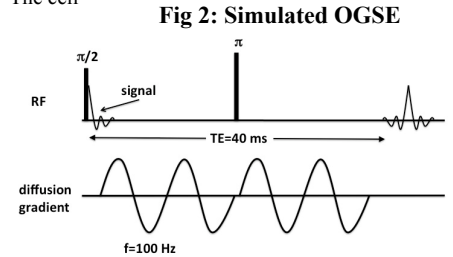
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Introduction: Recent interest in oscillating gradient spin echo (OGSE) sequences for DWI contrast in tumors is due to the fact that they are capable of probing diffusion times on the order of 1 ms, while conventional pulsed gradient spin echo (PGSE) methods are limited to diffusion times on the order of 10 ms. Thus, OGSE contrast may be based on intracellular changes associated with cancer, such as the known increase in nucleus-to-cell volume ratio (NCR) which scales with tumor grade. In this work, we use a Monte Carlo simulation of diffusion in a tissue model to 1) determine the behaviour of healthy/malignant contrast with OGSE frequency, 2) determine the contribution of NCR-mediated contrast to total contrast, which includes the effects of changes in cell volume fraction (CVF), or cellularity, often associated with malignancy, and 3) determine whether the contrast frequency response can be predicted using a calculated effective diffusion coefficient dependent on diffusion time.

Methods: The tissue model consists of packed cells modeled as concentric nested spheres as shown in Fig 1. The inner sphere represents the nucleus. Physiological values are used for diffusion coefficients and membrane permeabilities [1]. The cell



radius is fixed at 5 μm. NCR is determined by the nuclear radius, and CVF is determined by the distance between cell centers. Healthy tissue is modeled with CVF=0.26 [2] and NCR=5% [3]. Malignant tissue is modeled with CVF's of 0.54 [2] and 0.74 (most tightly-packed case) and with NCR's of 20%, 33% and 45% [3]. The model is incorporated into a modified version of the Camino DWI simulation and analysis toolkit [4]. A typical simulated OGSE is shown in Fig 2. OGSE sequences all have TE=40 ms. Monte Carlo simulations of random spin motion are performed with time steps of 0.004 ms. An effective diffusion coefficient, $D_{eff}(t_D)$, dependent upon diffusion time, t_D , is calculated for our model using Sen's method for cell-like compartments separated by a semipermeable membrane [5]. The diffusion-attenuated signal, $S(t_D)$, is then given by $S(t_D)/S_0 = \exp(-bD_{eff}(t_D))$, where S_0 is the signal with no diffusion gradient, and b is a function of the OGSE parameters [1].



Results: Fig 3 shows contrast as a function of OGSE frequency for gradient amplitudes 5 G/cm (typical of clinical scanners), 40 G/cm and 100 G/cm and for three different malignant NCR's. Solid lines show total contrast, and dotted lines show the NCR component of contrast. Fig 4 shows contrast for $G_{max}=100$ G/cm for malignant CVF's of 0.54 (red) and 0.74 (black). Again, total and NCR-mediated contrast are shown. Fig 5 shows signal and healthy/malignant contrast calculated using the calculated $D_{eff}(t_D)$ (CVF=0.74 for both healthy and malignant tissue).

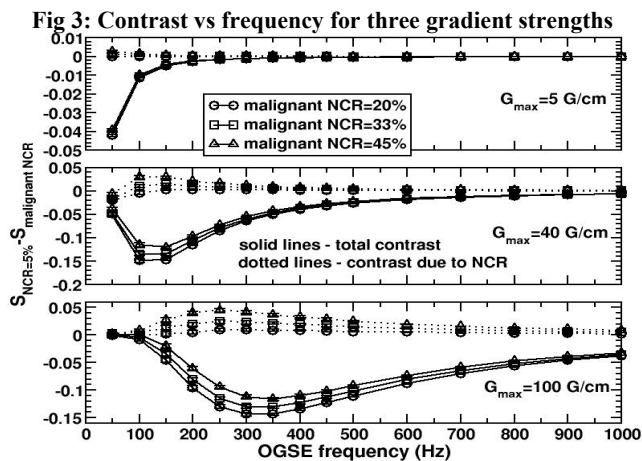
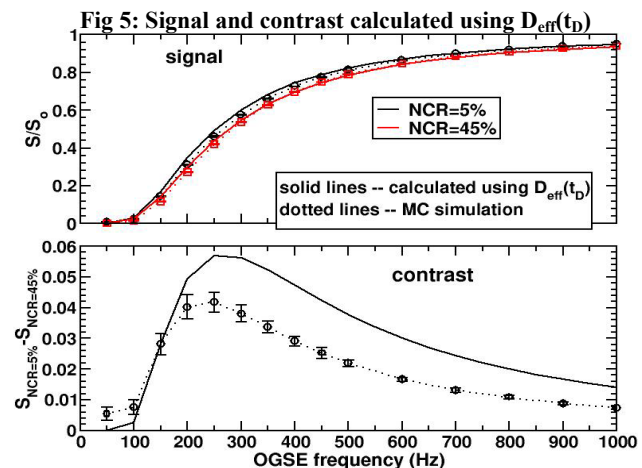
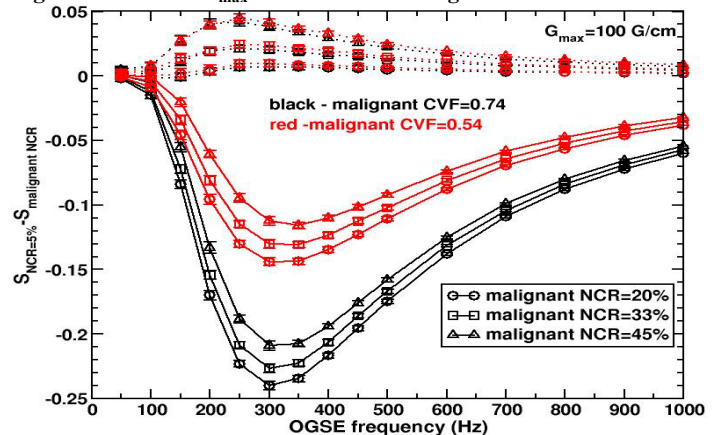


Fig 4: Contrast at $G_{max}=100$ G/cm for malignant CVF's of 0.54 and 0.74



Discussion:

- Contrast is dependent on OGSE frequency (Fig 3), with distinct frequency optima at which total contrast is maximized: *i.e.* 50 Hz at 5 G/cm, 150 Hz at 40 G/cm, 350 Hz at 100 G/cm. The optima for NCR and total contrast differ at 100 G/cm.
- NCR contrast is significant, especially at 40 G/cm and 100 G/cm where it amounts to up to 30% of the total contrast (Fig 3). NCR contrast has the opposite sign of total contrast, and, thus, works to decrease the overall contrast.
- NCR contrast is insensitive to the malignant CVF (Fig 4, dotted lines), indicating that diffusion between the cellular and extracellular environments plays little role.
- At high gradient frequencies (> 1000 Hz) NCR contrast is insignificant, and contrast is due only to CVF (Fig 4).
- $D_{eff}(t_D)$ is capable of qualitatively predicting the frequency response of contrast, including the optimum frequency (Fig 5 lower panel). However, the calculation cannot replicate all dynamics, resulting in significant quantitative differences.

References: 1 Xu J, Does MG, Gore JC. *Mag Res Med* 61:828-833 (2009); 2 Gibbs P et al, *Investigative Radiol* 44:572-576 (200); 3 Helpap B, Virchow Arch. 393:205-214 (1981); 4 Hall MG, Alexander DC. *IEEE Trans Med Imag* 28:1354-1364 (2009); 5 Sen PN, *J Chem Phys* 119:9871-9876 (2003).