Mapping ^{129}Xenon ADC of Radiation-Induced Lung Injury at Low Magnetic Field Strength Using a Sectoral Approach

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TARGET AUDIENCE: Hyperpolarized Xenon-129 MRI of the lung.

INTRODUCTION: Hyperpolarized xenon gas (^{129}Xe) MRI is an emerging technique that permits direct visualization of lung anatomy and function. In particular, the apparent diffusion coefficient (ADC) of ^{129}Xe has been shown to be a sensitive indicator of microanatomical changes associated with lung inflammation, including radiation-induced lung injury [1]. Furthermore, the magnetization available from hyperpolarization is independent of MRI magnetic field strength, providing images at field strengths substantially lower (<1 T) than typically used clinically [2]. Due to reduced susceptibility effects, low field strengths also offer substantially increased T_2* in the lung which can be exploited to reduce bandwidth and/or increase coverage of *k*-space following an RF pulse. In this work, a pulse sequence is developed for hyperpolarized ^{129}Xe lung imaging at 0.074 T based on a pseudo non-Cartesian (i.e. *Sectoral*) *k*-space trajectory (**Fig. 1**) [3], and compared to conventional Cartesian imaging using fast gradient recalled echoes. A diffusion-weighted version of the *Sectoral* approach is also developed and used to measure and map ^{129}Xe ADC at 0.074 T in both healthy rats and rats with radiation-induced lung injury (i.e. pneumonitis) confirmed by histology.

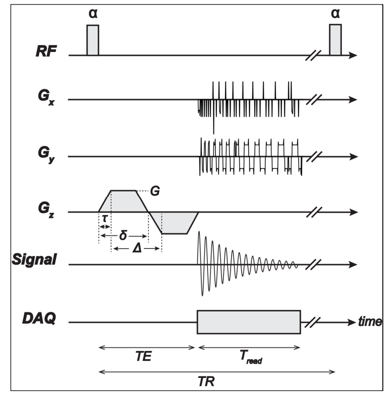

Figure 1: *Sectoral* pulse sequence including a diffusion-weighted bipolar trapezoidal pulse with diffusion time, ***Δ***, lobe duration, ***δ***, ramp time, ***τ***, and gradient magnitude, ***G***.

METHODS: *All procedures followed animal use protocols approved by Western University's Animal Use Subcommittees*. MRI was performed using a custom-built resistive magnetic MRI system [4] at 0.074 T and custom-built saddle RF coil [5] tuned to the resonance frequency of ^{129}Xe (0.883 MHz). Naturally abundant ^{129}Xe was hyperpolarized (~5 % polarization) using an in-house continuous flow spin exchange optical pumping system. The *Sectoral* pulse sequence parameters were: *# RF pulses*=16, *FOV*=95×95 mm^2, $\Delta x \times \Delta y$=1.49×1.49 mm^2, *matrix size*=64×64 *TR*/*TE*=10/3 ms, T_{read}=128.9 ms, *BW*=11.1 kHz, *b*=0 and 17.0 s/cm^2, *diffusion time*=2.4 ms. The RF pulses followed a variable flip angle trajectory as previously described [6]. SNR efficiency based on phantom image SNR, resolution, scan time and bandwidth of *Sectoral* and FGRE was used to compare image quality (**Table 1**). Four Sprague-Dawley rats (~444 g) were irradiated uniformly to the chest with a total dose of 14 Gy for 14 minutes at a dose rate of 134±1 cGy/min. Five rats served as healthy controls. ^{129}Xe *Sectoral in vivo* lung imaging was performed 2-weeks post irradiation using an MRI-compatible mechanical ventilator (PIP=16 cm H_2O, TV=2.6 ml) following 4 wash-out breaths of ^{129}Xe. A multi-breath *Sectoral* approach was used to achieve greater signal during diffusion-weighting by acquiring a part of *k*-space (i.e. a sector) following a separate ^{129}Xe gas inhalation. After euthanasia, the lungs were prepared for histological analysis. The mean linear intercept (L_m) was calculated on a 4×3 grid by dividing the total of the line lengths by the total number of intercepts. The mean ADC map values were then compared with L_m for both cohorts as well as the full width at half maximum of the ADC histograms derived from the maps (ADC_{FWHM}).

RESULTS AND DISCUSSION: **Table 1** summarizes the SNR efficiency calculations from FGRE and *Sectoral* phantom images. **Fig. 2(a)** shows ADC_{FWHM} values for all the rats revealing a significant separation between healthy and irradiated lungs (p=0.0317). The increase in ADC_{FWHM} following irradiation is likely attributable to heterogeneous injury response by the lung and/or differences in the time course of the injury. **Fig. 2(b)** shows the mean ADC values for each rat versus the corresponding L_m values measured from histology indicating a significant correlation (p=0.0061**)**. The positive linear correlation (r^2 = 0.74) between ^{129}Xe ADC and L_m, reflects that *Sectoral* diffusion MRI with ^{129}Xe is sensitive to changes in lung morphology associated with radiation pneumonitis. This work demonstrates the feasibility of hyperpolarized ^{129}Xe lung MRI in rodents at very low magnetic field strength using the *Sectoral* approach. Furthermore, ADC mapping using *Sectoral* is also feasible and can be used to detect radiation-pneumonitis at an early enough stage to effect changes in treatment.

Table 1: Summary of ^{129}Xe phantom SNR efficiencies.

	FGRE	*Sectoral*
SNR Efficiency	2.8	5.8

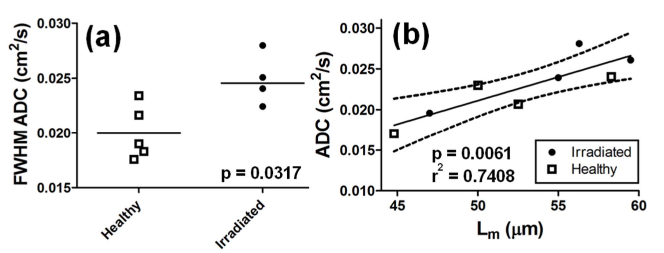

Figure 2: **(a)** FWHM ADC values for healthy and irradiated cohorts. **(b)** Linear regression fit for ADC vs. L_m.

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