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

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MOTIVATION

- ***In vivo*** **imaging with hyperpolarized ^{129}Xe gas enables the regional anatomical and functional evaluation of lung disease. For example, the apparent diffusion coefficient (ADC) of ^{129}Xe gas has been shown to be useful for detection of emphysema and radiation-induced lung injury (RILI) [1].**
- **Hyperpolarization is independent of the MRI static field and therefore, low field strengths can be exploited for imaging to reduce costs while maintaining good image quality [2].**
- **A pseudo non-Cartesian pulse sequence, which is the frequency encode *Sectoral* (Fig. 1) extension of the phase-encoding Sectoral-SPRITE sequence [3], may be optimal for low field ^{129}Xe MRI as it requires only a few (e.g. 16) RF pulses and thereby makes efficient use of the non-renewable magnetization. In addition, *Sectoral* reduces diffusion weighting and takes advantage of the long apparent transverse relaxation time (T_2*) available at low fields compared to conventional Cartesian approaches (i.e. Fast Gradient Recalled Echo (FGRE)).**

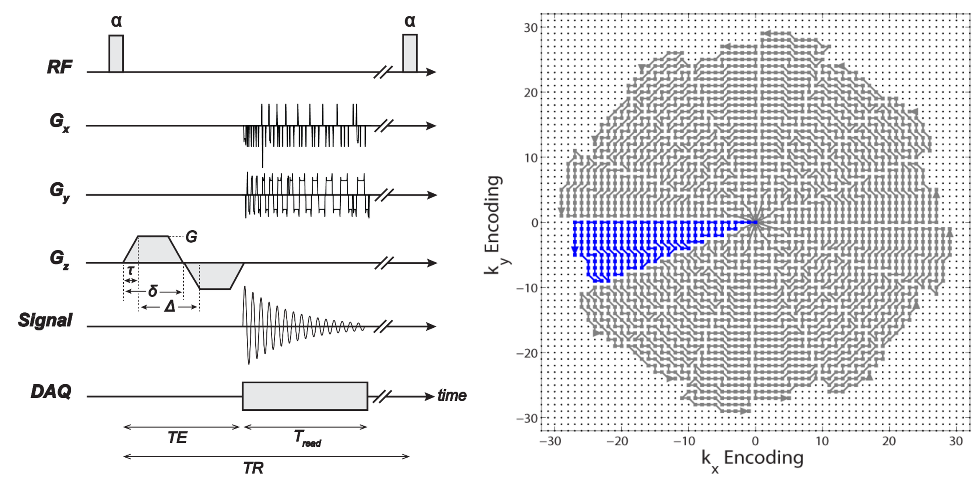

Figure 1: (left) The *Sectoral* pulse sequence for the acquisition of one sector. It includes a bipolar trapezoidal gradient pulse with diffusion time, *Δ*, lobe duration, *δ*, ramp time, *r*, and gradient magnitude, *G*. The X and Y gradients are then applied throughout signal acquisition. (right) The sequence is repeated for all 16 sectors with the *k*-space traversal trajectory.

HYPOTHESIS

(1) Sectoral ^{129}Xe imaging at low field will provide improved SNR efficiency compared to conventional FGRE.

(2) Regional ^{129}Xe ADC changes will be measurable in a RILI rodent model, consistent with histology.

METHODS

PHANTOM AND ANIMAL PREPARATION

This study was approved by the Western University Council on Animal Care.

- **For all *in vitro* measurements, either a flow through syringe and hallow acrylic resolution phantom (33 mL) were used.**
- **For *in vivo* imaging, rats were tracheostomized with an endotracheal tube and ventilated with custom ventilator (Fig. 2).**
- **To induce RILI, 4 male Sprague Dawley rats irradiated (14 Gy) with Cobalt-60 irradiator and incubated 2 weeks. 5 aged-matched un-irradiated served as healthy control.**

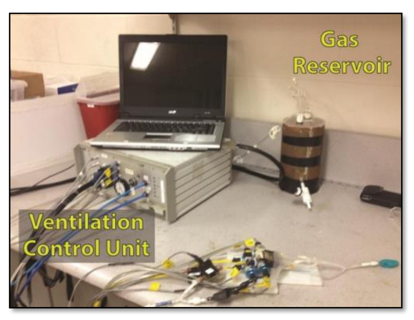

Figure 2: Custom ventilator control unit with gas reservoir.

METHODS

MRI HARDWARE

- **All images were acquired with a custom-built, 0.07 T resistive magnet (Fig. 3) [2]. Imaging samples were placed in a transmit-only/receive-only saddle coil (Fig. 3) tuned to the resonance frequency of ^{1}H (3.163 MHz) or ^{129}Xe (883 kHz).**
- **Naturally abundant ^{129}Xe gas was hyperpolarized using a preclinical continuous flow xenon polarizer. Estimated polarization, before freeze-thaw, was approximately 5%.**

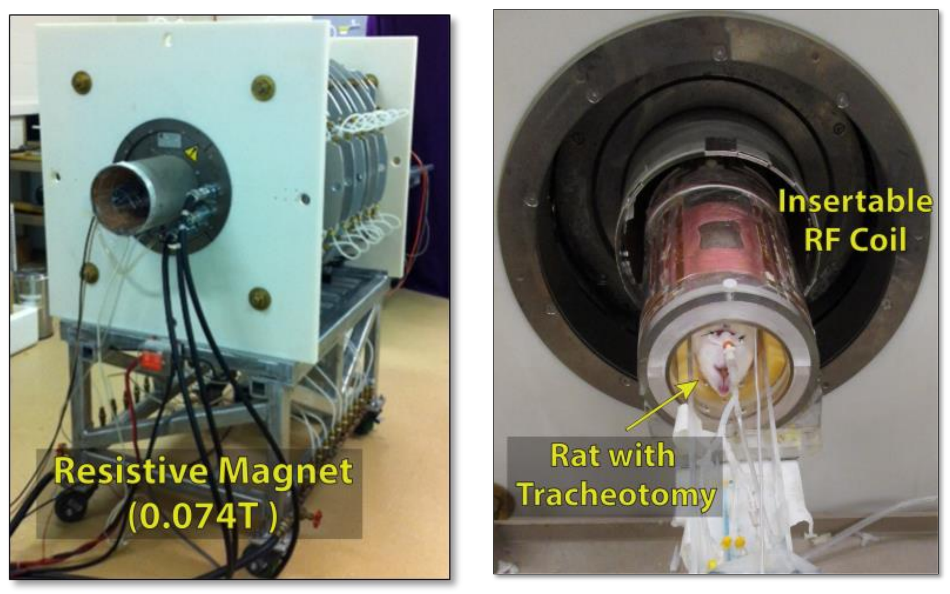

Figure 3: (left) 0.07 T MRI system and (right) RF coil with rat tuned to 0.883 MHz.

SECTORAL PULSE SEQUENCE

- **The *Sectoral* sequence used 16 RF pulses to fill *k*-space in 16 sectors with the following parameters: FOV = 94×94 mm^2, Δx and Δy = 1.4×1.4 mm^2, TR/TE = 13/3 ms, Δt = 90 μs, T_{read} = 129 ms, BW = 11.1 kHz.**
- **The FGRE pulse sequence parameters were: 64 RF pulses, FOV = 85×85 mm^2, Δx and Δy = 1.18×1.18 mm^2, TR/TE = 10/4.8 ms, Δt = 20 μs, T_{read} = 12.8 ms and BW = 50 kHz.**
- **The duration of each RF pulse was determined by a variable flip angle scheme [4] to ensure complete and uniform consumption of magnetization by the end of the 16 RF pulses.**
- **The gradient waveforms were mapped with the pure phase encode magnetic field monitoring technique [5] to ensure that the *Sectoral* gradient waveforms were properly balanced.**
- **The *Sectoral* sequence was modified to obtain diffusion-weighted images (b_1 = 0 and b_2 = 17.0) and diffusion time of 4.8 ms.**

DATA ANALYSIS

- **All *Sectoral* image data were processed using MATLAB (Mathworks, USA).**
- **ADC maps were calculated on a pixel-by-pixel basis using:**

$$S_i = S_0 \cdot \exp(b \cdot ADC)$$

where S_0 is a scaling constant.

- **Image quality was compared by SNR efficiency:**

$$\frac{SNR}{(\Delta x \cdot \Delta y) \times \sqrt{t \cdot BW}}$$

- **Post-mortem, the removed animal lungs were infused with formalin, cut into 5 μm slices, and stained with H&E.**
- **The mean linear intercept (L_m) was calculated on a 4x3 grid by:**

$$L_m = \frac{l}{N_i}$$

where *l* is the line length and Ni is the number of counted intercepts. L_m was then compared with ADC values.

RESULTS

IN VITRO

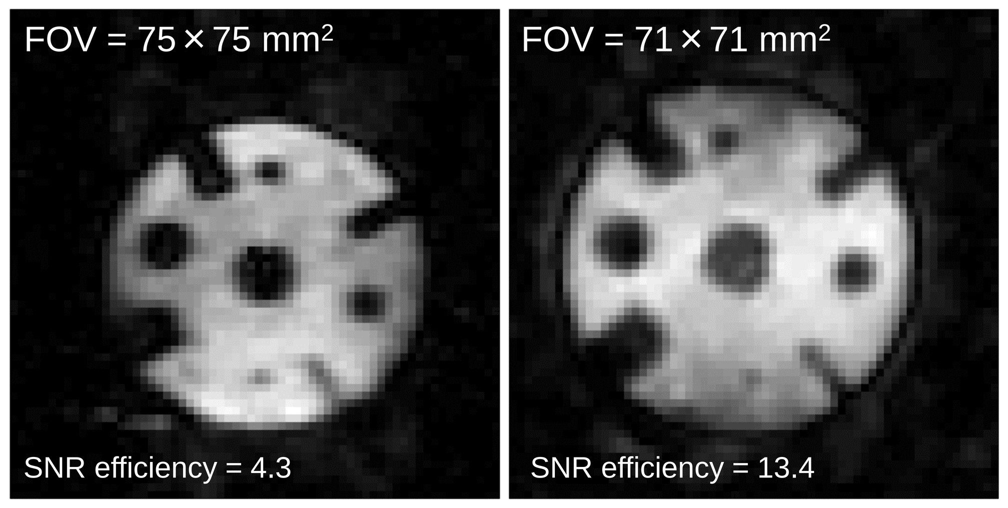

Figure 4: Representative ^{1}H images of proton resolution phantom FGRE (left) and *Sectoral* (right).

Table 1: Summary of ^{129}Xe syringe phantom imaging results

	FGRE	*Sectoral*
Resolution (mm²)	1.33	1.47
FOV (mm²)	85	94
BW (kHz)	50	11.1
Scan Time (s)	1.5	2.2
SNR	42.8	61.1
SNR efficiency	2.8	5.8

IN VIVO

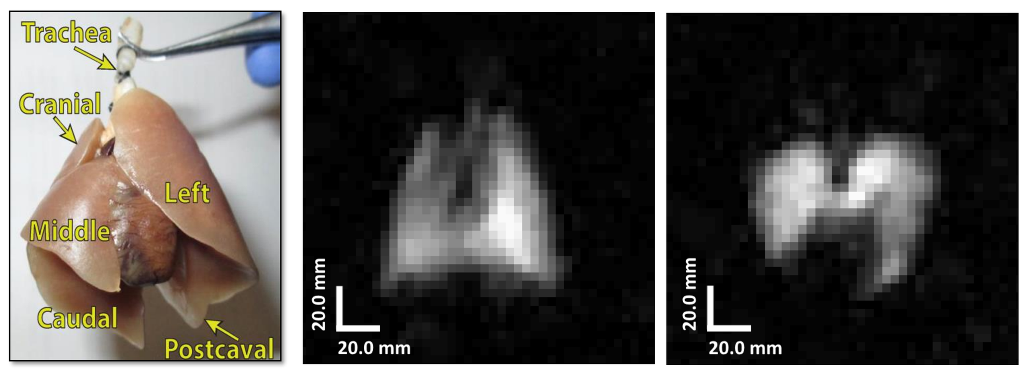

Figure 6: Photograph of a rat lung (left). Representative *Sectoral* 2-D whole-lung projection image of a rat lung in coronal view (middle) and axial view (right) obtained at low field with ^{129}Xe. FOV = 112×112 mm^2.

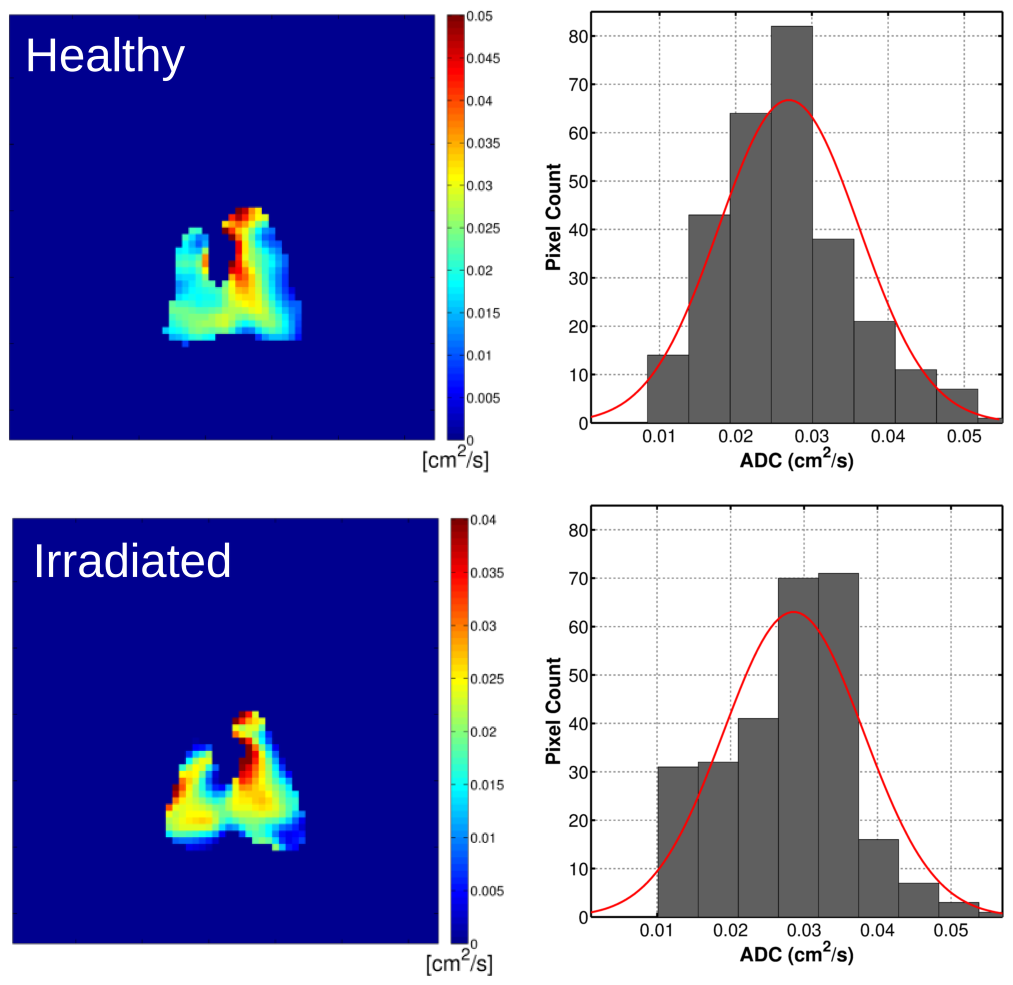

Figure 7: Representative rat lung ADC-maps for healthy (top-left) with corresponding histogram (top-right) and irradiated (bottom-left) with corresponding histogram (bottom-right).

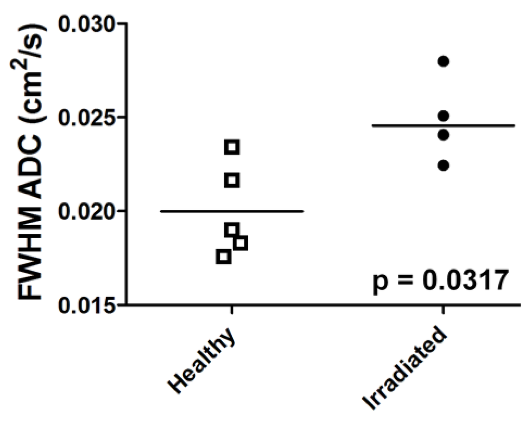

Figure 8: Full width at half maximum (FWHM) ADC values for healthy and irradiated cohorts. Results are obtained using a two-tailed (Mann Whitney) unpaired t-test. The calculated p = 0.0317.

RESULTS

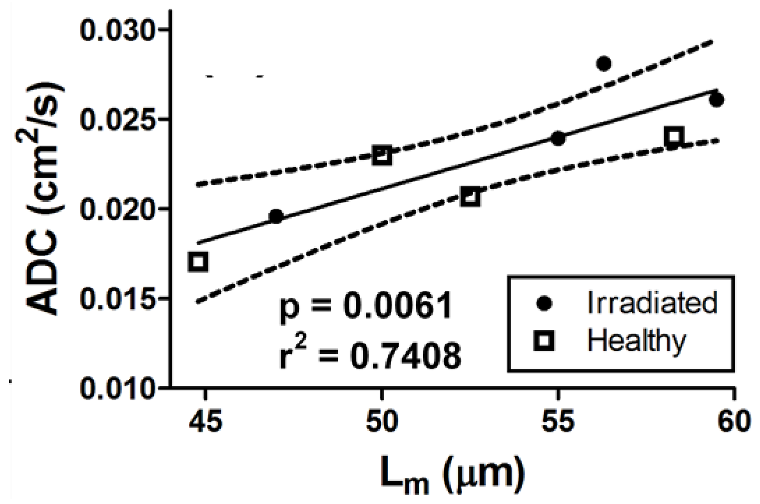

Figure 9: Summary of data obtained for 8 lung specimens (4 healthy, 4 irradiated). Each data point is a mean calculated across all imaging pixels for a given ADC map. The horizontal axis shows L_m obtained from direct histological measurements on the same lungs.

DISCUSSION

- ***Sectoral* is a promising technique for hyperpolarized ^{129}Xe lung MRI at low magnetic field strength (0.07 T) and may also be applicable at clinical field strengths (3 T) depending on T_2* and available gradient performance.**
- ***Sectoral* imaging showed 2 times more favourable improvement in SNR efficiency over FGRE imaging.**
- **A significant difference was observed between irradiated and healthy rat lungs by extracting the ADC values measured by *Sectoral* diffusion-weighting. Positive correlation between ^{129}Xe diffusivity and L_m reflects that *Sectoral* diffusion MRI with ^{129}Xe may be sensitive to the geometry of the individual alveoli.**
- **Structural and functional lung parameters, including ADC, are obtainable with the *Sectoral* imaging sequence and agree reasonably well with values expected for healthy rat [1].**
- **The use of higher polarization and enriched ^{129}Xe gas now available from commercial polarizers is expected to improve these results further.**
- **The work presented here forms the basis for future *in vivo Sectoral* studies of rodent lungs of specific disease models such as Radiation Induced Lung Injury (RILI) and emphysema.**

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