Mapping of $^{129}$Xe Apparent Diffusion Coefficient Anisotropy in Radiation-Induced Lung Injury
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Introduction: Magnetic Resonance (MR) imaging of hyperpolarized noble gases ($^1$He and $^{129}$Xe) provides anatomical and functional information about the lungs. In particular the $^{129}$Xe apparent diffusion coefficient (ADC) can be used to detect alveolar enlargement due to emphysema (1). ADC in the lung is anisotropic and can be described by two components; (i) a longitudinal coefficient ($D_T$) representing diffusion along the terminal bronchiole and (ii) a transverse coefficient ($D_R$) representing diffusion perpendicular to the terminal airway (2). $^1$He $D_T$ has been shown to be particularly sensitive to alveolar damage in a rat model of emphysema involving elastase instillation (3). $^{129}$Xe ADC anisotropy may also be useful for early detection of alveolar shrinkage due to radiation induced lung injury (RILI), a significant complication associated with radiotherapy treatment of lung cancer. In this work, $^{129}$Xe gas ADC anisotropy was mapped in the lungs of a cohort of rats receiving irradiation and compared to histology.

Methods: All procedures followed animal care protocols approved by the University of Western Ontario (ACVS) and were consistent with procedures used by the Canadian Council on Animal Care (CCAC). Sprague Dawley rats (~350g) were irradiated with a dose of 18Gy using a $^{60}$Co source collimated to expose the right lung only. The rats were imaged two weeks following irradiation. Prior to imaging, the animals were anesthetized, intubated and mechanically ventilated using an MR-compatible ventilator. Breath-hold 2D diffusion-weighted imaging (FOV 5x5cm; Matrix size 64x64; TE 10.3ms; TR 15ms; BW 2kHz, VFA) was performed at 3T (MR-750, GEHC), using a high-performance insertable gradient system, following four breaths of pure hyperpolarized xenon gas (80% enriched in $^{129}$Xe) polarized to approximately 10% (XeBox-E10, Xemed LLC, Durham NH). The diffusion-sensitization gradient pulse had a ramp up/down time of 500 μs, constant time of 2000 μs and a diffusion time of 5 ms; providing eight b values ranging from 0 to 115 s/cm. The diffusion time of 5 ms was chosen to give best $^{129}$Xe ADC sensitivity to alveolar length scales based on simulations (4). Following ADC mapping, the rat lungs were removed, fixed, sectioned and stained for histological analysis.

Results: The anisotropic diffusion equation (3) was fit to the data using a non-linear least square algorithm (lsqcurvefit.m, Matlab, The Mathworks, Natick MA) to extract mean, longitudinal and transverse diffusion coefficients ($\overline{D}$, $D_T$, and $D_R$), on a pixel-by-pixel basis. Figure 1 shows representative maps of $\overline{D}$ and $D_T$ respectively for a healthy rat (a, b) and an irradiated rat (c, d). Figure 2 shows the corresponding $D_T$ histograms for the whole-lung for these same rats. Table 1 summarizes the whole-lung $D_T$ and $D_R$ results for all rats. Histology confirmed the presence of RILI within both lungs in the irradiated rats.

Discussion: Mapping of $^{129}$Xe ADC anisotropy resulted in greater discrimination of radiation-induced lung injury compared to mean ADC maps. Specifically, the transverse diffusion coefficient ($D_R$) was observed to decrease in the irradiated rat cohort as early as two weeks post-irradiation. These changes are consistent with reductions in alveolar radii seen with histology and likely arise from inflammation and/or edema characteristic of the early radiation pneumonitis (RP) stages of RILI. The detection of RILI within both lungs was unexpected. With concurrent developments in clinical hyperpolarized $^{129}$Xe imaging, these results are expected to be translatable to human studies in future. Clinically, detection of regional RP may be helpful in order to adjust the radiotherapy fractionation scheme and/or conformation field and/or apply adjuvant therapy to mitigate the effects of RILI.

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References: