# Detecting Radiation-Induced Lung Injuries using XTC MRI: Initial Findings

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**Introduction:** The treatment of lung cancer with radiation therapy frequently leads to radiation-induced pulmonary injury surrounding the targeted tumor site. In clinical practice two phases of lung injury can be distinguished: early pneumonitis and late fibrosis (1). In this preliminary study we used a rabbit model to investigate whether Xenon polarization Transfer Contrast (XTC) MRI (2-4) provides sufficient sensitivity to track the regional changes in lung function over four months following stereotactic lung radiosurgery. Our findings were compared to CT studies and to histological results after the animals were euthanized 4 months after radiosurgery.

**Methods:** Experiments were performed on a 1.5-T commercial whole-body imager (Sonata, Siemens Medical Solutions, Malvern, PA) using a custom-made transmit-receive birdcage RF coil (IGC Medical Advances, Milwaukee, WI). The two imaging segments of the XTC acquisition were asymmetric FLASH sequences (75% of *k*-space sampled) with excitation flip angles of 3.6° and 10.1°. The following sequence parameters were used: non-selective excitation with a 160µs Gaussian RF pulse; matrix size 64×64; TR/TE 7.9/3.8 ms; FOV 190 mm; receiver bandwidth 260 Hz/pixel. The two FLASH image acquisitions were separated by a series of 22 contrast-generating 180°/-180° RF pulse pairs with an inter-pulse delay of 40ms applied at the dissolved-phase resonance frequency of 202 ppm for the XTC experiment or at -202ppm for the control experiment. Two New Zealand rabbits (4-5kg) were irradiated with 3 fractions of 20Gy (6MV stereotactic radiosurgery to a 1.6cc volume in the right mid lung) delivered by a Hi-Art Helical TomoTherapy machine (Helical Tomotherapy, Madison, WI). Before and approximately 4, 8, 12 and 16 weeks after irradiation the animals were anesthetized with a mixture of Xylazine/Ketamine and intubated before undergoing MR imaging. The animals were ventilated with 50cc of isotopically enriched (85% $^{129}$Xe) xenon gas, polarized to approximately 10-15% via spin exchange with an optically pumped rubidium vapor (Model IGI 9600Xe Xenon Polarizer, MITI, Durham, NC). The polarizer had been optimized to increase the achievable polarization levels. Immediately after the MRI scan at week 16, the rabbits were euthanized, their lungs harvested and fixed in a 10% formalin solution. Six tissue samples were obtained from each lung. Each sample was processed, cut in 5µm thick slices, stained with H&E and photographed with a high-resolution digital camera. The protocol was approved by our Institutional Animal Care and Use Committee.

**Results:** Figure 1 depicts the target area for radiation treatment (Fig. 1A) and the resulting lung injury as assessed by XTC MRI, CT and histology. In both animals the gas-phase depolarization maps that were derived from the XTC MRI data sets showed the development of a large region with reduced depolarization values after approximately 3 months. The region coincided very well with the radiation treatment target area and the depolarization maps were consistent with initial inflammation in rabbit #2 followed by a reduction in lung tissue volume of up to 30% (rabbit #1). Histology confirmed this region to contain enlarged alveolar structures and to be depleted of blood vessels. The findings for both rabbits were qualitatively similar but the overall radiation injury appeared to be of lesser extent in rabbit #1. The CT images indicated the development of radiation-induced pneumonitis in the early weeks after irradiation (rabbit #2 only) and exhibited a hyperlucent region with a drop in image intensity of up to 40% after about 4 months in both animals.

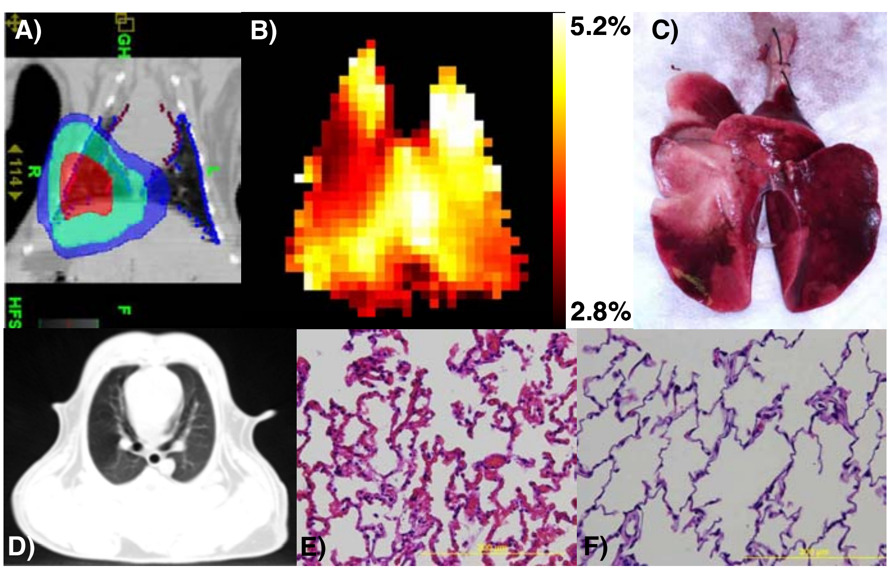


**Figure 1:** A) CT planning scan of the target area for irradiation (red: full dose, green: 50% dose, blue: 25% dose). B) Coronal lung-tissue-volume weighted depolarization map (low-pass filtered projection) obtained with XTC MRI, which shows reduced gas exchange in the irradiated area 4 months after treatment. C) Excised lung, which exhibits a "bleached" appearance in the irradiated section. D) Axial CT image that appears hyperlucent in the same region. E) Tissue sample from the untreated left lung. F) Tissue sample from the treated right lung. The alveoli are enlarged compared to the healthy lung. Although the irradiated lung tissue is alive (staining indicated active cell nuclei) it is mostly devoid of blood vessels. Results shown are from rabbit #1.

**Conclusion:** The high sensitivity of epithelial cells to radiation makes blood vessels very susceptible to radiation damage. By choosing a sufficiently long delay time (~40ms) between the contrast-generating RF inversion pulse pairs the depolarization maps obtained from XTC MRI data sets become highly correlated with the volume of lung tissue compartments involved in gas exchange (3). The sensitivity of this technique is sufficient to detect radiation-induced changes in the lung structure of rabbits due to inflammation and tissue breakdown as confirmed by CT imaging and histology. Thus, XTC MRI has the potential to track changes in lung function in radiotherapy patients and may facilitate future modifications in the treatment procedures to minimize the resulting radiation damage to the lung.

**References**

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