

Assessment of tumor physiological changes following hypo-fractionated SBRT using multi-parametric MRI

Heling Zhou¹, Rebecca Denney¹, Zhang Zhang², Debabrata Saha², and Ralph P Mason¹

¹Radiology, University of Texas Southwestern Medical Center, Dallas, TX, United States, ²Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX, United States

Purpose: It is recognized that oxygenation plays an important role in the effectiveness of radiation therapy (1). Hypofractionated stereotactic body radiation therapy (SBRT) has shown promising results in clinical trials, but may be particularly susceptible to hypoxia resistance. Historical evidence has suggested that reoxygenation occurs during conventionally fractionated therapy, but there is less opportunity during a hypofractionated course and timing could be critical. The ability to assess oxygenation accompanying radiation therapy should enhance treatment planning. In this study, we performed blood oxygen level dependent (BOLD) and tissue oxygen level dependent (TOLD) MRI together with dynamic contrast enhanced (DCE) MRI at different time points with respect to irradiation of human lung cancer xenografts in a subcutaneous rat model.

Methods: A549 human lung cancer (3×10^6) cells were implanted subcutaneously in the thigh of nude rats. When the tumor volume reached approximately 0.5 cm^3 , baseline MRI was initialized at 4.7 T. Interleaved BOLD (multi-echo gradient echo; TR = 150ms, ten echo times from 6 to 69 ms, flip angle = 20°) and TOLD (gradient echo; TR/TE = 30/5ms, flip angle = 45°) MRI were acquired with the intervention of oxygen challenge (from air to 100% O_2). DCE (spin echo; TR/TE = 200/15ms) was performed with iv injection of gadolinium contrast (Gadovist) at a dose 0.1mmol/kg body weight. T_1 map (spin echo; TE= 20 ms, TR= 0.1, 0.2, 0.3, 0.5, 0.7, 0.9, 1.5, 2.5, 3.5 s) were also acquired for pharmacokinetic analysis of DCE prior to contrast injection. Each tumor received three doses of 12 Gy each (once a week) with oxygen breathing 30 minutes pre and during the radiation. MRI was performed same day prior to, and 24, 48 hours and one week after the first SBRT treatment. The tumor volume was measured by caliper every week to determine the tumor growth delay. Data were processed using Matlab. Semi-quantitative percentage signal intensity changes (% Δ SI) of BOLD and TOLD and quantitative T_1 and T_2^* maps were calculated. Initial area under the curve (IAUC), time-to-maximum (TTM) and slope were calculated from DCE. The Yankeelov model was used for the quantitative analysis to obtain K_{trans} and v_e (2).

Results: Three doses of 12 Gy showed effective tumor growth control on all the animals. Intra-tumor heterogeneity was revealed on multi-parametric maps, especially in BOLD, T_2^* and DCE, which may indicate the special growth pattern of A549 subcutaneous tumors (Fig. 1). % Δ SI of BOLD and TOLD as well as T_2^* while breathing air and oxygen all decreased over the course of the treatment, which may imply decreased oxygenation in tumor (Fig. 2). % Δ SI of BOLD and TOLD of the different scans of the same animal

appeared to be strongly correlated, but the trend was quite different between animals (Fig. 3). No obvious changes were observed among the DCE parameters.

Conclusions: Multi-parametric MRI revealed longitudinal changes in the tumor microenvironment. The changes in BOLD and TOLD may allow optimized timing of hypo-fractionated SBRT. Further exploration with more animals and different time points will be valuable to better understand the effect of radiation therapy and help optimize the interval of the treatments.

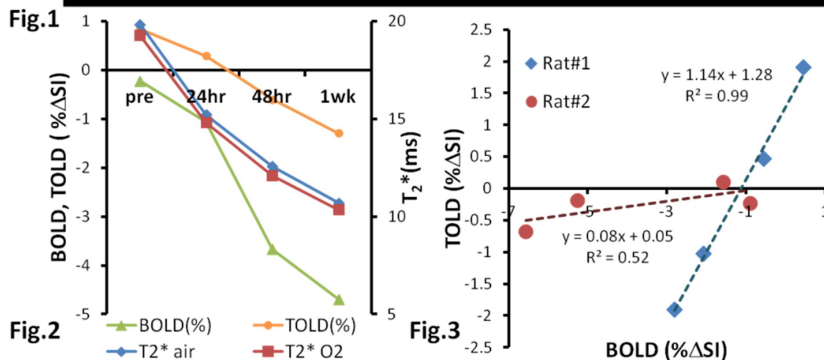
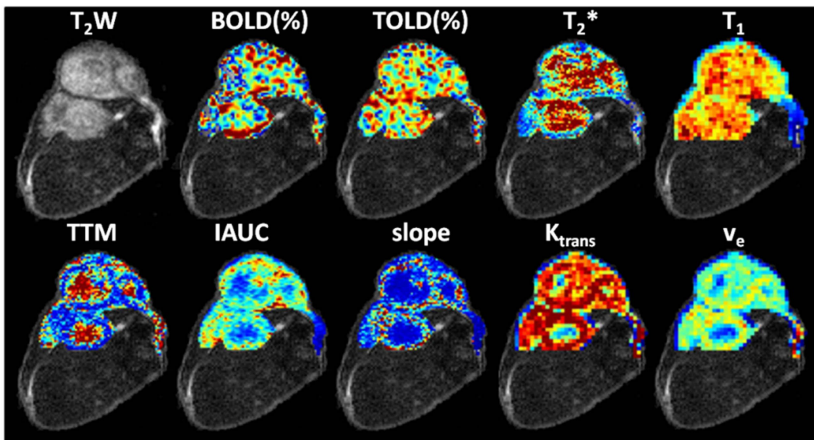


Fig. 1. T_2 weighted image and multi-parametric maps of one representative animal before treatment. **Fig. 2.** Changes of BOLD % Δ SI, TOLD % Δ SI, T_2^* values over the course of treatment. **Fig. 3.** Correlation of BOLD % Δ SI and TOLD % Δ SI of two rats.

References: 1. *Int. J. Radiat Biol.* (2006). 82:699; 2. *Phys. Med. Biol.* (2008). 53:2617