Detecting Early Tumor Response of Prostate Cancer to Radiation Therapy using Multi-Parametric 14T 1H and Hyperpolarized 13C MR Imaging

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Introduction: Radiation therapy remains one of the most common definite treatments for prostate cancer, but despite excellent survival rates, a significant number of patients suffer post-treatment cancer recurrence. Clinical dose-escalation trials reported that higher radiation doses significantly improve biochemical control and clinical disease-free survival for locally advanced prostate cancer patients [1]. The purpose of this study was to investigate early response to the impact of increasing doses of radiation therapy in TRAMP tumors using multi-parametric 14T 1H & hyperpolarized (HP) 13C MR imaging.

Methods: A TRAMP mouse tumor (size = 3.5cc) was exposed to varying doses of radiation as shown in Fig. 1 [2]. Imaging studies were performed on a 14T, 600WB micro-imaging spectrometer (Varian Inc.). Diffusion weighted imaging (DWI) data were acquired using a spin-echo pulse sequence (TE/TR=20ms/1.2s, 0.156x0.312x1mm). [1-13]Pyruvate and [13C]Urea were hyperpolarized and 3D imaging data were acquired as described previously [2,3]. Following injection of Gd-DTPA (Magnevist, Bayer HealthCare), dynamic contrast enhancement imaging (DCE) was acquired using a T1-weighted gradient echo sequence (TE/TR=1.11/39ms, 0.312x0.312x1mm). The signal intensity of HP urea was normalized to maximum HP urea in the kidney.

Result: Fig. 2 shows lac/pyr ratio, urea, area under curve (AUC) calculated from DCE and ADC images overlaid on T2-weighted images at baseline, 1, 4, and 8 days after radiation therapy. Fig. 3 provides a quantitative summary from high (14-8Gy) and low dose (8-4 Gy) regions of tumor at 1 to 8 days after treatment. Both HP markers showed significant dose dependent changes over time (p<0.01). Lac/pyr ratio from high dose region decreased by day 1 after treatment and continued to decrease on day 4 & 8 (p<0.01 compare to day 0). While lac/pyr ratio from low dose region initially increased by day 1, and subsequently decreased by day 4 & 8 compare to day 0 (p<0.01). HP urea from the high dose region showed significant decrease 1 day after therapy (p<0.01), and subsequently returned to baseline level. HP urea from low dose level significantly increased on day 1 and continued to increase (p<0.01). AUC calculated from 1H DCE showed similar result as HP urea. DCE AUC from high dose region significantly decrease on day 1 after treatment and returned to baseline level over time. Whereas DCE AUC from low dose region continuously increased over time (p<0.01), ADC from both high and low dose regions initially decreased and returned to baseline level and higher by day 8 following treatment.

Discussion: These results suggest HP biomarkers are sensitive to the early changes in metabolism and perfusion in tumor exposed to varying radiation dose levels. HP 13C biomarkers correlated with conventional 1H MR markers. Ongoing studies are investigating the ability of multi-parametric 1H and HP 13C MR in planning and monitoring of prostate cancer radiation therapy.

Fig. 1: Dose distribution diagram overlaid on the MR axial image of TRAMP mouse tumor

Fig. 2: Lac/pyr (A), urea (B), DCE AUC (C) and ADC (D) images from day 0, 1, 4, and 8 days after radiation therapy

Fig. 3: % change from baseline of lac/pyr (A), urea (B), ADC (C) & DCE AUC (D) from 1-8 days after treatment in tumor regions receiving high (red) and low (blue) dose radiation. *: Significantly different from baseline level. +: Significantly different between high and low dose regions.


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