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

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Introduction: Radiation therapy remains one of the most common definite treatments for prostate cancer, but despite excellent success 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 ^{1}H & hyperpolarized (HP) ^{13}C 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}C]pyruvate and ^{13}C 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 T_1-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.

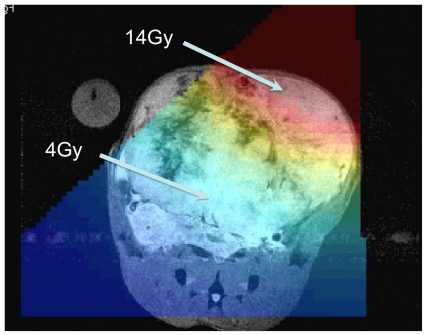

Fig. 1: Dose distribution diagram overlaid on the MR axial image of TRAMP mouse tumor

Result: Fig. 2 shows lac/pyr ratio, urea, area under curve (AUC) calculated from DCE and ADC images overlaid on T_2- 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 ^{1}H 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 ^{13}C biomarkers correlated with conventional ^{1}H MR markers. Ongoing studies are investigating the ability of multi-parametric ^{1}H and HP ^{13}C MR in planning and monitoring of prostate cancer radiation therapy.

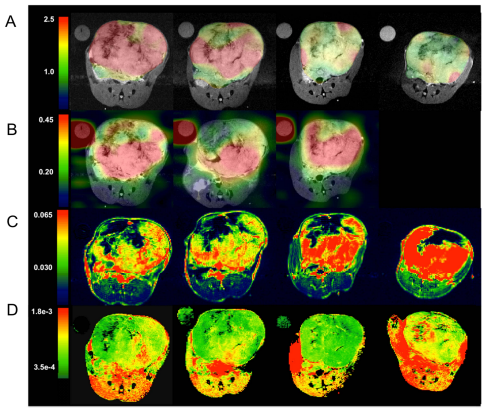

Fig. 2: Lac/pyr (A), urea (B), DCE AUC (C) and ADC (D) images from day 0, 1, 4, and 8 days after radiation therapy

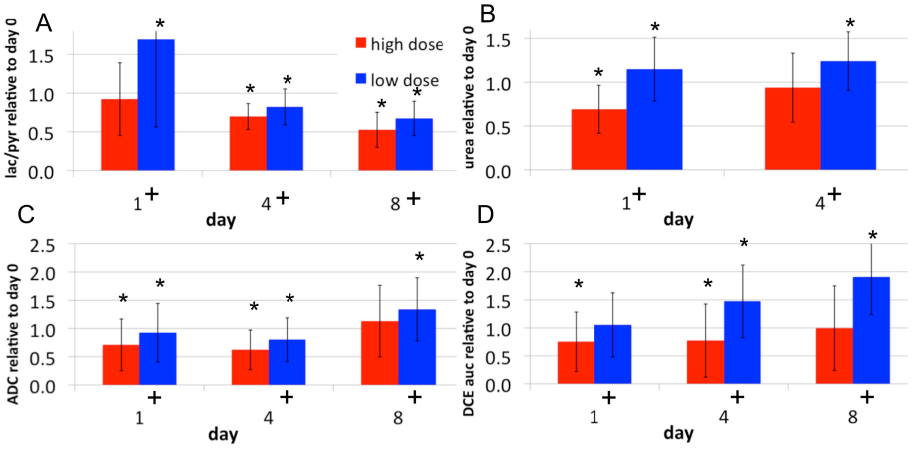

Fig 3: % change from baseline of lac/pyr (A), urea (B), ADC (C) & DCE AUC (D) from 1-8 days after treatment in tumor regions receiving high (red) and low (blue) dose radiation. *: Significantly different from baseline level. +: Significantly different between high and lose dose regions.

Reference: 1. Martinez AA, *et. al.* Int. J. Radiation Oncology Biol. 2011;79(2):363-370 2. Zhang VY *et. al.* Proceedings of the 19th Annual Meeting of ISMRM, Montreal, 2011, p3161. 3. Sukumar S *et. al.* Proceedings of the 19th Annual Meeting of ISMRM, Montreal, 2011, p3531

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