Assessing the utility of Oxygen-Enhanced Magnetic Resonance Imaging (OE-MRI) to predict radiation response of rat prostate Tumors

Derek A White[1,2], Zhang Zhang[3], Heling Zhou[1], Debu Saha[3], Peter Peschke[4], Zhongwei Zhang[1], and Ralph P Mason[5]

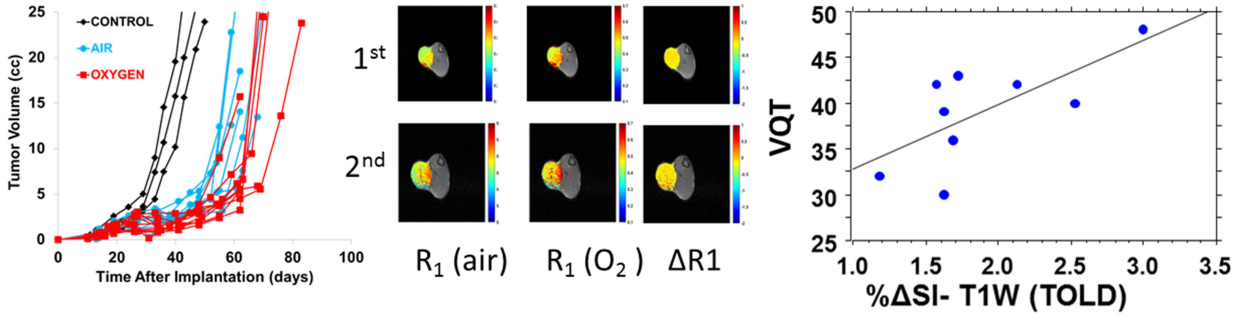
[1]*Radiology, University of Texas Southwestern, Dallas, Texas, United States,* [2]*Bioengineering, University of Texas at Arlington, Texas, United States,* [3]*Radiation Oncology, University of Texas Southwestern, Dallas, Texas, United States,* [4]*Clinical Cooperation Unit Molecular Radiooncology, German Cancer Center, Heidelberg, Germany,* [5]*Radiology, University of Texas Southwestern, Dallas, TX, United States*

TARGET AUDIENCE: Radiation Oncologists, Medical Physicists and those interested in prognostic biomarkers of therapy response.

PURPOSE: To evaluate correlations of oxygen sensitive MRI parameters (R_1, R_2*) with radiation response in syngeneic rat prostate tumors. There is increasing interest in the utility of MRI to predict radiation response with methods showing more or less robust correlations in diverse tumor types. It was recently reported that ΔR_1, but not ΔR_2* in response to a pre-irradiation oxygen breathing challenge was related to growth delay in small rat prostate tumor with respect to a single high dose of radiation (MRM 71, 1863 (2014)). We have now explored this observation for a split dose regimen, to more closely reproduce the potential clinical application.

METHODS: Subcutaneous syngeneic Dunning prostate R3327-AT1 tumors were implanted in adult male rats (*n* = 21). An interleaved blood-oxygen level dependent (BOLD) and tissue-oxygen level dependent (TOLD) dynamic data acquisition (or IBT) was performed using air as a baseline with oxygen as a breathing challenge. A 2-D multi-slice spoiled gradient-echo with multi-echo sequence was used to evaluate tumor ROI BOLD %ΔSI, as well as quantitative ΔR_2* with respect to oxygen breathing challenge. TOLD used a 2-D multi-slice spoiled gradient-echo sequence to calculate the T_1weighted %ΔSI in response to inhaling oxygen. Quantitative R_1 maps were additionally acquired during air and O_2 breathing to determine ΔR_1 values. Tumors were irradiated with a split dose of two fractions (each 15 Gy) one week apart. OE-MRI was repeated before the 2nd dose. Tumor growth was observed to provide tumor volume doubling (VDT) and quadrupling (VQT) times. Pearson correlation analysis on the OE-MRI biomarkers was assessed for predicting tumor growth delay measured as the time for tumors to quadruple (VQT).

RESULTS: There was a general correlation between %ΔSI BOLD and TOLD response before the first irradiation (R^2>0.4), but not 2nd dose. 15 or 18 tumors showed a greater TOLD signal response to oxygen breathing one week after the first irradiation, which was significant for the tumors on rats breathing O_2 ($p<0.02$). VDT and VQT were significantly longer for tumors on rats breathing O_2 than air ($p< 0.05$). A correlation was found between the VQT and ΔR_1 determined prior to the first radiation dose (R^2>0.4 for rats breathing O_2 and R^2>0.7 for air). There was also a correlation between ΔR_2* prior to first dose and VDT for rats breathing O_2 (R^2>0.4). No such correlations were found with respect to the second dose. However, there was a correlation between the T_1W signal response prior to the 2nd dose and VQT



Left) Tumor growth curves with respect to split dose irradiation (total 30 Gy) for tumors receiving sham irradiation or while rats breathed air or O_2. Center) R_1 maps for a representative tumor before 1st and 2nd radiation doses while breathing air and O_2 and showing difference. Right) Time to quadruple in volume following IR for tumors on rats breathing O_2 showed a trend with T_1W ΔSI (TOLD) observed before the second radiation dose.

DISCUSSION: Hypoxia is known to influence radiation response and thus the ability to measure hypoxia and its potential modification are important. These results demonstrate that Dunning prostate R3327-AT1 tumors experience tumor growth delay following split dose irradiation, which is greater when rats breathe oxygen. However, there is extensive variation in the response. Most tumors showed a larger R_1 response to O_2-breathing challenge after the first irradiation consistent with reoxygenation. The time to quadruple in volume was correlated with R_1 response measured prior to the first dose for tumors on rats breathing air or oxygen. VQT was related to the change in T_1w signal response with respect to oxygen challenge prior to the 2nd dose. If R_1 and T_1W are indeed a function of tumor pO_2, as suggested by several reports then such measurements should assist in developing enhanced radiation treatment plans.

ACKNOWLEDGEMENT: Supported in part by R01 CA139043, 1P30 CA142543, and P41 EB015908.