Comparison of Tumor Perfusion Measured by Hyperpolarized ^{13}C Urea with DCE MR Imaging Prior to and Following Radiation Therapy

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Purpose: Dynamic contrast-enhanced magnetic resonance imaging (DCE MRI) has shown great clinical potential for assessing prostate cancer presence and aggressiveness prior to and after radiation therapy (1). Metabolically-inactive hyperpolarized (HP) urea is a nontoxic, endogenous agent that enables MR imaging of perfusion based on a direct signal source that is background-free. Co-polarization of ^{13}C pyruvate and urea also allows the simultaneous assessment of tumor perfusion and metabolism in a single MR acquisition (2,3). However, whether hyperpolarized ^{13}C urea provides the same information as DCE MRI remains to be answered. To address this question, this study investigated tumor perfusion prior to therapy and following radiation therapy in a transgenic murine model of prostate cancer using both HP ^{13}C urea and DCE MRI.

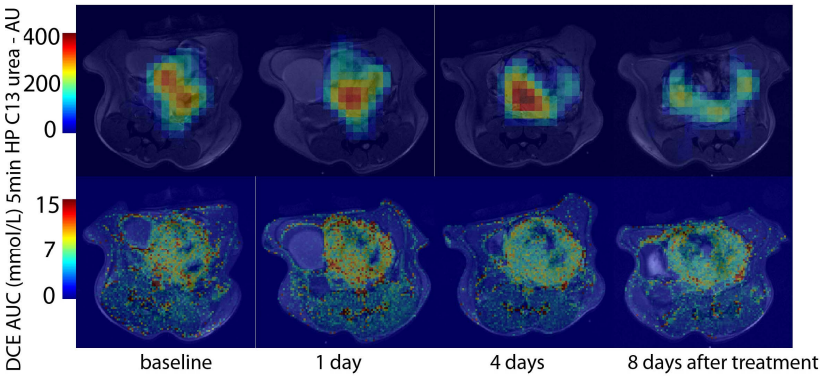

Fig. 1: HP ^{13}C urea and DCE-AUC from day 0, 1, 4, and 8 days after treatment.

Methods: Four transgenic TRAMP mouse prostate tumors (size = 2.1±1.1cc) were scanned at pre-treatment, and 1, 4, and 8 days after radiation therapy. Animals were treated with HDR brachytherapy (Ir-192), which resulted in a dose distribution within the tumor where ventral side of the tumor exposed to a higher dose at 14 Gy, and dorsal side exposed to a lower dose of 4 Gy. Imaging studies were performed on a 14T, 600WB micro-imaging spectrometer (Varian Inc.) [1-^{13}C]pyruvic acid and ^{13}C urea were co-hyperpolarized and 3D imaging data were acquired as described (4). Immediately after image acquisition, a series of non-selective 90° saturation pulses were applied to destroy residual ^{13}C signal within the animal. A 2nd injection of the remaining hyperpolarized mixture was injected into a tube placed inside the coil, and a ^{13}C spectrum was acquired to estimate % polarization. Urea data was normalized to the % polarization. Following Gd-DTPA (Magnevist, Bayer HealthCare), dynamic contrast enhancement imaging (DCE) was acquired using a T_1-wt gradient echo sequence (TE/TR=1.11/39ms, 0.312x0.312x1.25mm, acquired over 5 min). Area under curve (AUC), initial enhancement slope, and washout slope were calculated from DCE images.

Correlation Coefficient (R) with HP urea	Pre-treatment	Day 1	Day 4	Day 8
DCE-MRI AUC	0.50	0.57	0.51	0.52
DCE-MRI Initial slope	0.51	0.50	0.46	0.42
DCE-MRI Washout slope	0.41	0.39	0.32	0.38

Table 1: correlation coefficients comparing HP ^{13}C urea with DCE-MRI parameters, at pre-treatment, 1 day 4 days and 8 days after treatment. **P-value < 0.01** for all comparisons.

Results: Fig. 1 shows ^{13}C urea and DCE AUC images overlaid on a TRAMP tumor prior to and 1, 4, and 8 days after radiation therapy. HP ^{13}C urea was acquired at lower in-plane resolution (1.25x1.25x1.25 mm) compare to DCE MRI. Visually, normalized HP ^{13}C urea signal intensity spatially correlated with the AUC of the DCE MRI signal intensity at all time points investigated. Significant correlations were found between HP ^{13}C urea and DCE AUC, initial slope, and washout slope at all time points (Table 1). The washout slope had the weakest correlation compared to HP urea (Table 1), and there was an indication that there may be some additional information in the DCE wash-out data that was not captured by the HP ^{13}C data.

Discussion & Conclusion: Significant correlations were found between ^{13}C urea and DCE MR data at baseline and following radiation therapy, indicating that hyperpolarized ^{13}C urea MRI provides similar information as DCE MRI. This finding is of clinical importance since ^{13}C urea has a very good safety profile and could be co-polarized with ^{13}C pyruvate to provide a simultaneous measurement of perfusion and metabolism in patients without the nephrotocixity concerns associated with Gd-based contrast agents. However, future studies will need to investigate the acuracy of combined ^{13}C pyruvate and ^{13}C urea in determining cancer presence and grade relative to DCE MRI prior to and after therapy.

Reference: 1. Hara N, et al. Prostate. 2005; 62(2),140-147. 2. Wilson DM, et. al. J Magn Reson 2010;205:141-147. 3. Von Morze C. Magn Reson Med 2012;30:305-311. 4. Sukumar S, et. al. Proceedings of the 19th Annual Meeting of ISMRM, Montreal, 2011, p3531

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