A SPATIALLY RESOLVED EVALUATION OF RADIATION INDUCED METABOLIC RESPONSE IN NORMAL AND MALIGNANT LIVER WITH 3D ^{31}P MRSI

Scott Jones[1,2], Anshuman Panda[1,2], Higinia Cardenes[3], James Fletcher[2], Gary Hutchins[2], and Ulrike Dydak[1,2]

[1]*School of Health Sciences, Purdue University, West Lafayette, Indiana, United States,* [2]*Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indianapolis, IN, United States,* [3]*Department of Radiation Oncology, Indiana University School of Medicine, Indianapolis, IN, United States*

Introduction: While surgical intervention is the gold standard for curative treatment of Hepatocellular carcinoma (HCC), over 80% of all cases presented to the clinic are considered inoperable (1). Stereotactic body radiotherapy (SBRT), a highly conformal and non-invasive external beam therapy has been shown to be an effective alternative for non-surgical candidates (2). However, the liver's hypersensitivity to ionizing radiation can result in potentially fatal complications (radiation-induced liver disease) and therefore is a limiting factor in deciding the appropriate therapeutic dose. The ability to evaluate the *in-vivo* radiobiological response of both the tumor and normal liver tissue would be an important first step in defining dose re-optimization strategies based on an individual patient's response. Cell energy and phospholipid metabolism, as measured by ^{31}P MRS, has been shown to not only discriminate well between healthy and malignant liver tissue (3; 4), but also to detect the first signs of such a biological response to ionizing radiation in animals within only days of radiation exposure (5; 6). Therefore, the purpose of this abstract is to show the preliminary results of a newly developed 3D ^{31}P magnetic resonance spectroscopic imaging (MRSI) protocol using a dual-tuned (^{1}H/^{31}P) multi-channel coil (7) to characterize the spatially resolved biochemical alterations to normal liver and tumor, following the first treatment fraction with SBRT.

Materials and Methods: Two patients (n=2) diagnosed with liver confined HCC were recruited to date, for this IRB approved study and written informed consent was obtained. Pre- and post-treatment ^{31}P MRSI scans were acquired about 24 hours prior to and 24 hours after the first SBRT treatment fraction (14 Gy), respectively. All 3D ^{31}P spectroscopic imaging data were acquired on a 3T whole body MRI scanner (MAGNETOM Tim-Trio, Siemens Healthcare, Germany) using a dual tuned ^{31}P/^{1}H 8-channel phased array coil (8) and a 3D CSI-FID pulse sequence (TR/TE: 1000 ms/ 2.3 ms, bandwidth: 5000 Hz, 2048 data points/4096 with oversampling). A 400 mm x 400 mm x 200 mm field of view (FOV) was phase encoded to 16 x 16 x 8 matrix resulting in a nominal voxel size of 2.5 cm x 2.5 cm x 2.5 cm or 15.63 cm^3. Weighted averaging (12 averages) was applied resulting in a total acquisition time of about 32 minutes. Metabolite signals were quantified with jMRUI (9) using the AMARES algorithm in MRSI mode (10) .

Results: Figure 1 shows one of eight slices of the 3D data set: an overall increase of β-ATP 24 hours post treatment in the entire axial liver slice is observed; except for a clear decrease at/near the tumor site (radiation target) when compared to the SBRT treatment plan. Figure 2 shows the response to radiation therapy for two representative spectra (slice 4; a normal liver voxel (PME/PDE = 0.62) and a tumor liver voxel (PME/PDE=1.72)). The y-axes are always in institutional units, but are scaled equal for comparison. It can be seen that while the metabolism in the normal liver voxel does not change much (or slightly increases), metabolism in the tumor voxel is drastically reduced, also reflected in the β-ATP map in Fig 1.

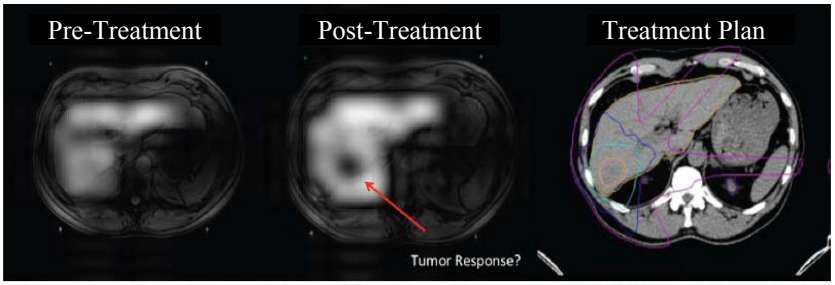

Figure 1: *β-ATP maps from pre- and post SBRT treatment and associated treatment plan.*

Discussion and Conclusion: We present preliminary data of a study in which we evaluate the utility of using 3D ^{31}P MRSI combined with a dual tuned (^{31}P/^{1}H) multi-channel liver coil to characterize the spatially resolved biochemical alterations to normal liver and associated tumor, following the first SBRT treatment fraction. While this study is still ongoing, the results presented here suggest that the radiation induced metabolic response of both normal and malignant liver tissue can not only be detected, but also spatially differentiated by 3D ^{31}P MRSI at 24 hours post treatment. Therefore, we conclude that evaluating the radiobiological response of the whole liver with 3D ^{31}P MRSI is feasible and has the potential to significantly increase our understanding of the variability in radiation dose-response in the liver. Data acquisition in several more patients is ongoing. *The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.*

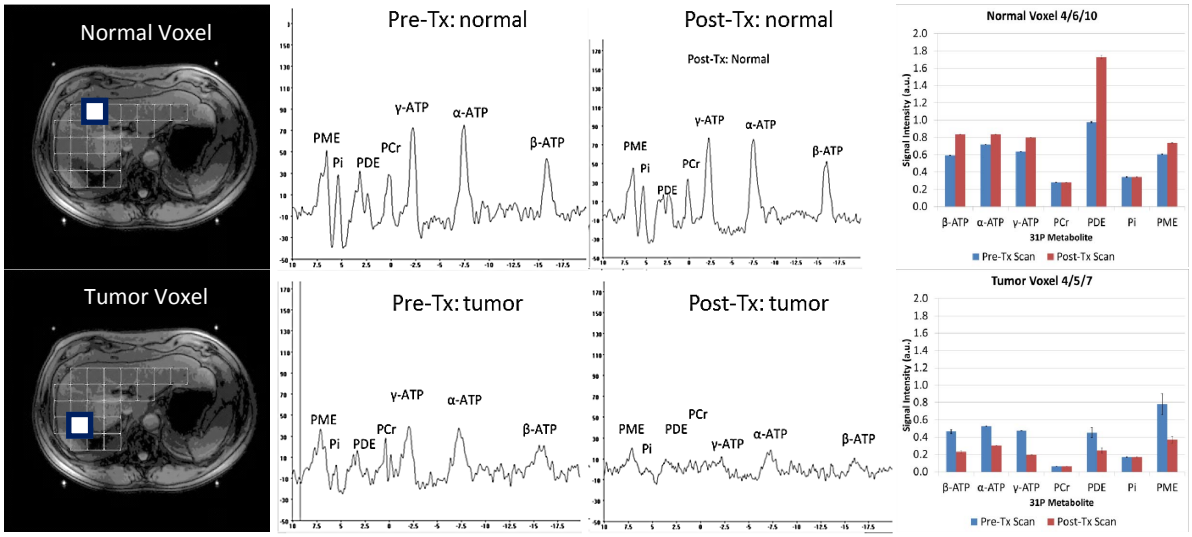

Figure 2: *Pre- and post-treatment changes in ^{31}P metabolite signals shown for normal liver voxel and tumor voxel.*

References:

[1] J.H. Liu, et. al., Annals of Surgical Oncology 11 (2004) 298-303. [2] D.L. Andolino, et. al., Int. J. Radiat. Oncol. Biol. Phys. (2011). [3] I.J. Cox, et. al., Journal of Hepatology 14 (1992) 265-275. [4] A. Panda, et. al., AAPM Conference, 2010, 3470. [5] R.-S. Yu, World Journal of Gastroenterology 15 (2009) 2723. [6] M. Sentjurc, e. al., Radiology and Oncology 44 (2010) 174-179. [7] S. Jones, et. al., Proceedings 19th ISMRM, Montreal, Quebec, 2011. [8] A. Panda, et. al., Proceedings 17th ISMRM, Honolulu, 2009, [9] A. Naressi, et. al., MAGMA 12 (2001) 141-52. [10] D. Stefan, et. al., Measurement Science and Technology 20 (2009) 104035