Serial Imaging of Physiological and Metabolic Changes in Response to Radiotherapy with Tumor-Bearing Mice

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[TARGET AUDIENCE] This presentation targets those who are interested in tumor oxygenation imaging and specialized in DNP-MRI. [PURPOSE] Cancer cells harbored within hypoxic regions try to survive the hypoxic microenvironment by preserving limited amount of oxygen and generate energy by not only mitochondrial oxidative phosphorylation but also glycolysis. Herein, a non-invasive co-imaging system of an electron paramagnetic resonance imaging (EPRI) of absolute partial pressure of oxygen (pO_2) and ^{13}C magnetic resonance imaging (MRI) of hyperpolarized [1-^{13}C] pyruvate metabolism[1,2] was developed to visualize the correlation between tumor oxygen status and energy metabolism. [METHODS] SCCVII and HT29 solid tumors were formed by injecting 5×10^5 cells and 1×10^6 cells s.c. into the right hind legs of mice. After the animal was placed in the resonator that was used as an identical coil for EPRI and 7 T MRI operating at 300 MHz. Hyperpolarized [1-^{13}C] MRI studies were performed with the echo-planar spectroscopic images (EPSI). We investigated the effect of single 5 Gy irradiation on the relationship between tumor pO_2 and energy metabolism by co-imaging of EPRI and hyperpolarized ^{13}C MRI in HT29 tumors. [RESULTS] Feasibility of this serial imaging of pO_2 and hyperpolarized ^{13}C MRI was demonstrated in the three-tube phantom containing different concentration of [1-^{13}C] pyruvate, [1-^{13}C] lactate, and oxygen, and in mice bearing two difference tumor lines. SCCVII tumor has significantly larger hypoxic sub-region (pO_2 < 8 mmHg) than HT29 tumor that is supported by higher blood perfusion in HT29 tumors. The flux of ^{13}C labeled pyruvate-to-lactate conversion was higher in SCCVII than HT29, consistent with tumor oxygenation status. Lactate/pyruvate ratio in 0-8mmHg of 1 day after 5Gy irradiation of HT29 tumor (76%) is higher than of non irradiation of HT29 tumor (36%), suggesting that the enzymatic conversion of pyruvate to lactate is much higher in 0-8 mmHg of 1 day after 5Gy irradiation of HT29 tumor. [DISCUSSION] Pyruvate-to-lactate flux was significantly higher 1 day post radiation especially in hypoxic sub-regions that is explained by decreased perfusion, decreased tumor pO_2, and increased extracellular acidification rate. [CONCLUSION] This new approach of cancer imaging will provide a temporal window for a new perspective in molecular imaging for radiation therapy. [REFERENCES] 1. Matsumoto S, Hyodo F, Subramanian S, et al. Low-field paramagnetic resonance imaging of tumor oxygenation and glycolytic activity in mice. J Clin Invest 2008; 118: 1965-73. 2. Day SE, Kettunen MI, Gallagher FA, et al. Detecting tumor response to treatment using hyperpolarized 13C magnetic resonance imaging and spectroscopy. Nat Med 2007; 13: 1382-7.