Abstract

Understanding the dynamic nature of tumor hypoxia is vital for cancer therapy. The presence of oxygen within a tumor during radiation therapy increases the likelihood of local control. A novel interstitial diffuse optical probe was designed and used to make real-time measurements of blood volume fraction and hemoglobin oxygen saturation within a tumor with a high temporal resolution. The device uses the technique of optical fiber spectroscopy to fit a measured light spectrum onto a diffusion equation. It uses a library of absorption coefficients of known chromophores to determine their concentration in a medium.

The device was initially tested in milk solutions to distinguish between the relative fat concentrations. Animal fat absorption coefficients were successfully used to distinguish between the relative fat concentrations in different solutions of powdered milk. Hemoglobin oxygen saturation measurements were performed using a customized vessel designed to control hemoglobin oxygen saturation and blood volume in a solution of blood with different concentrations of an oxygen scavenger, tetrakis (hydroxymethyl) phosphonium chloride. The optical device was found to measure the changes in oxygen saturation in this chamber consistently, and the measurements correlated with the concentration of the oxygen scavenger that was added in the blood solution.

In near-simultaneous measurements of blood volume and oxygen saturation in tumor-bearing mice, the changes in blood volume and oxygen saturation measured with the interstitial diffuse optical probe were benchmarked against measurement from a photoacoustic (PA) imaging system. Positive correlations between the device and the PA imaging system in measured blood

volume and oxygen saturation were observed. Similar measurements were performed simultaneously between the device and blood oxygen level-dependent magnetic resonance image (BOLD-MRI), and correlations were also observed.

In the process of characterizing tumor microenvironment, coherent oscillations in hemoglobin saturation dynamics in T24 and FaDu cell line xenograft models of the bladder and head and neck squamous cell carcinoma, respectively, were observed using BOLD-MRI and PA imaging. It was posited that the well-established biochemical nonlinear oscillatory mechanism called the glycolytic oscillator was a potential cause of the coherent oscillations in tumors. These data suggest that metabolic changes within individual tumor cells may affect the local tumor microenvironment, including oxygen availability and therefore radiosensitivity. These individual cells could synchronize the oscillations in patches of similar intermediate glucose levels.

No acute temporal effects of 2, 4, and 10 Gy ionizing radiation on hemodynamics were observed in tumor microenvironment from measurements with the optical device. The results of a real-time modulation of radiation based on oxygen availability in a tumor to improve local control, remained inconclusive when the optical device was used in FaDu cell tumor-bearing mice.