QUANTITATIVE MEASUREMENT OF TUMOR HYPOXIA RESPONSE TO MILD TEMPERATURE HYPERTHERMIA TREATMENT IN HT29 TUMORS

Mutian Zhang

Graduate School of Arts and Sciences, Columbia University, New York, NY 10027

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E-mail: mz222@columbia.edu; mutian_zhang@hotmail.com

Dissertation Sponsor: John L. Humm, PhD, Department of Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY 10065

Quantitative measurements to detect tumor hypoxia response following a mild temperature hyperthermia treatment were conducted in rat HT29 xenografts. A hypoxia marker iodoazomycin galactopyranoside (IAZGP) was labeled with two radioisotopes of iodine ^{131}I and ^{123}I, which were injected into HT29 tumor-bearing nude rats 4-hour before and immediately after 41.5ºC, 45-munite hyperthermia treatment respectively. The animals were sacrificed 3-hour post hyperthermia, tumors resected, frozen and cryo-sectioned for digital autoradiography on phosphor imaging plate. Novel methods were developed to acquire and analyze the dual isotope digital autoradiographic images, to unfold the pixel contribution of tracers administered pre and post hyperthermia, thus providing quantitative information of the hypoxia change at the microscopic (50-micron) level. The results showed that, immediately following the hyperthermia treatment, there was a significant reduction in the tumor hypoxia fraction indicating that re-oxygenation had taken place in this rat HT29 xenograft model. Pixel-by-pixel analysis of the

data revealed a decline in hypoxia tracer uptake after hyperthermia in most regions, but with the concomitant emergence of some new regions of hypoxia identified by increased tracer uptake post treatment. In the body-temperature control group, the overall hypoxic fraction remained almost constant, with some hypoxic tracer redistribution (putative acute hypoxia) observed. In conclusion, the pre-treatment hypoxic fraction changed from between 18–42% to post-hyperthermia values of between 7%–20% (spread among 5 animals).