

AbstractID: 8217 Title: Effects of mild temperature hyperthermia on rat HT29 xenograft hypoxia measured with a dual-radiolabel hypoxia marker

Purpose: Quantitative measurements to directly determine the tumor hypoxia response following a mild temperature hyperthermia (MTH) treatment were conducted in a rat HT29 colorectal xenograft model.

Method and Materials: A hypoxia marker iodoazomycin galactopyranoside (IAZGP) was labeled with two radioisotopes of iodine ¹³¹I and ¹²³I. The two distinct IAZGP tracers were injected into HT29 tumor-bearing nude rats 4-hour before and immediately after 41.5°C, 45-minute 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 before and after hyperthermia, thus providing quantitative information of the hypoxia change at the microscopic (50-micron) level.

Results: The results showed that, immediately following MTH treatment, there was a significant reduction in hypoxia tracer binding, indicating a reduction in the tumor hypoxic fraction, and 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).

Conclusion: This study provided evidence for reoxygenation immediately following MTH treatment in the rat HT29 xenograft, with a preponderance of microscopic regional decreased radiotracer uptake. However, a few areas did exhibit increased hypoxia specific tracer uptake indicating the possible emergence of new hypoxia.