AbstractID: 8671 Title: A Mouse Model for Radiation-induced Disruption of the Blood-Brain Barrier

Purpose: The ability of radiation to disrupt the blood-brain barrier could be exploited therapeutically to enhance the delivery of drugs to tumors. The dynamic interplay between radiation and the delivery of therapeutic drugs of interest, however, is not well understood. We present a mouse model system which can be used to study these effects.

Materials & Methods: Two 1 mm-long microdialysis catheters were implanted into the mouse brain parenchyma or orthotopic tumor site. Using a precision radiation device developed by our group, we irradiated one catheter site while leaving the other as a control. Localization was accomplished via cone-beam CT guidance. Following radiation, we delivered temozolomide orally and then performed micro-dialysis fluid collection over a six hour period with an awake-animal system. Microdialysis provides a direct measurement of drug levels in the brain tissue via leakage across a porous membrane. Concentrations were measured by high-pressure liquid chromatography.

Results: Gafchromic EBT film measurements in phantoms demonstrate that for a local dose of 5 Gy to the catheter site, the contralateral control side receives less than 0.1 Gy. Catheter fiducials were visible in the cone-beam CT and were effectively used to localize radiation. Localized delivery can be validated with immunohistological staining for γH2Ax, a protein affected by double strand breaks. Concentrations of temozolomide were measured with a sensitivity of 0.02 μg/ml.

Conclusions: The system provides a highly accurate and direct means of examining the interaction between localized brain irradiation and drug delivery.