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Hypoxic radioresistance in particle minibeam tumor response: in vitro study to inform optimal peak dose and treatment planning protocols

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The existence of severe hypoxia in locally advanced tumors is well characterized. In terms of particle minibeam applications, few studies have considered the dose that may be required to completely sterilize tumor tissue that falls within the peak dose volumes. Instead, peak doses are mostly decided at random and dictated by valley dose treatment goals or anatomic constraints depending on the tumor position. Unfortunately, without thresholds/min/max data for each tumor type, the clinical team is left to design somewhat random treatment plans that do not account for important biology such as hypoxic resistance, vascular damage and indirect effects thereof, or intrinsic radiation resistance of each tumor type. We have begun a study to compare the hypoxic radiation response of F98 rat glioma cells when given graded doses of photons or protons in the Bragg peak or plateau regions to understand the predicted total single dose that would be required to eliminate all hypoxic cells. When this value is determined, beam width and spacing to allow desired valley doses for immune activation or other goals can be directly calculated and a consistent protocol for tumor treatment can be established. Our initial studies using photons suggest that while a dose of 15-20 Gy can eliminate over 8 logs of tumor cells in fully aerobic conditions, a dose of 90-100 Gy or more will be required to eliminate the same order of magnitude of hypoxic tumor cells in a peak dose volume. We surmise that protons of differing energies/dose rates that possess increased LET and RBE may allow the peak dose target to be reduced compared to photons. Plans to assess other particle minibeams with greater RBE with collaborating institutions and instrument platforms are underway.

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