

AbstractID: 6463 Title: Hypofractionation results in a decrease in tumor cell killing compared to standard fractionation as a result of tumor hypoxia

**Purpose:** Tumor hypoxia has been observed in many human cancers and has been shown to correlate with treatment failure in radiotherapy. The purpose of this study is to quantify the effect of radiation fractionation on tumor cell killing assuming a realistic distribution of tumor oxygenation and full reoxygenation between fractions. The sensitivity of the results to variations in the radiobiologically hypoxic fraction, the dose per fraction, and tumor cell intrinsic radiosensitivity is evaluated.

**Method and Materials:** A probability density function for the partial pressure of oxygen in a tumor cell population is quantified as a function of radial distance from the capillary wall. Estimates of the oxygen partial pressures for subpopulations of tumor cells are used to determine the corresponding oxygen enhancement ratios (*OERs*) for cell killing. The overall surviving fraction of a tumor cell population consisting of maximally resistant cells, cells at intermediate levels of hypoxia, and well-oxygenated cells is calculated as a function of dose per fraction for an equivalent tumor biological effective dose (BED).

**Results:** Our model predicts that tumor cell killing decreases by a factor of  $10^5$  over a radial distance of 130  $\mu\text{m}$  assuming a partial oxygen pressure of 60 mmHg at the capillary wall. For head and neck ( $\alpha/\beta = 10$  Gy) and prostate ( $\alpha/\beta = 3.0$  Gy) cancer, the surviving fraction of cells over a full treatment course increases by a factor of  $10^3$  as the dose per fraction is increased from 1–24 Gy and 1–18 Gy, respectively. The total dose delivered for each dose per fraction is calculated to achieve equivalent tumor BED values for reference head and neck and prostate treatments.

**Conclusion:** Hypofractionation of a radiotherapy regimen results in reduced tumor cell killing compared to conventional fractionation for tumors with regions of hypoxia.