AbstractID: 13764 Title: Dose and Dose Rate Effectiveness Factors (DDREF) for Fractionated Radiation Therapy

Purpose: Estimates of the DDREF are needed to better quantify the risks of second cancers arising from radiation therapy. Biologically motivated models to estimate the DDREF for fractionated radiation therapy treatments are developed and compared to data from the literature and to recommendations from the Biological Effects of Ionizing Radiation (BEIR) committee. **Methods:** Trends in cell death and neoplastic transformation are plausibly linked to the formation of small- and larger-scale DNA mutations. A linear-quadratic (LQ) model for radiation mutagenesis is used to estimate trends in cell transformation and death with dose, dose rate and dose fractionation. We assume that cancer incidence is proportional to the number of mutated or transformed cells, and derive isoeffect formulas to determine the DDREF for single- and fractionated doses. **Results:** The cancer incidence models accurately predict the bell-shaped dose-response curve for leukemia incidence in mice after an acute dose of radiation. For fractionated exposures, the dose-response curve for leukemia in mice becomes broader, giving the appearance of a plateau before decreasing towards zero for very large doses. For a single dose of low linear energy transfer (LET) radiation, the maximum DDREF of 2.5 is comparable to the factor of 2 recommended by the BEIR VII committee. For 2 Gy delivered in 35 fractions (57 mGy per fraction), the predicted DDREF is 1.05. For 35 fractions of 1 Gy, the DDREF is about 0.1, which implies that fractionated large doses of radiation are less biologically effective than a small, single dose of radiation. **Conclusion:** Models that correct for cell death after therapeutic doses are consistent with leukemia incidence in mice, as well as other published studies in animals and humans. The DDREF for fractionated radiation therapy may be substantially lower than the BEIR VII recommendation of 2 for low doses of low LET radiation.