AbstractID: 9423 Title: Computational Analysis of the Dose and Dose-Rate Dependence of DNA Double-Strand Break Repairs

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Computational Analysis of the Dose and Dose-Rate Dependence of DNA Double-Strand Break Repairs

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Purpose: Computational quantification of the dose and dose-rate dependence of radiation-induced DNA double-strand break (DSB) repair, and the significance of high dose and high dose-rate limits pertinent to stereotactic body radiation therapy (SBRT) fractionation regimens. **Materials and Methods:** The mass-action biochemical kinetics approach was used to describe the binding of repair enzymes to DSBs through the formation of intermediate repair complexes which lead to DNA rejoining. To quantify the formation of intermediate repair complexes, coupled non-linear ordinary differential equations (ODEs) which govern the dynamics of DNA DSB non-homologous end-joining (NHEJ) repair were used. Biochemical kinetics parameters for human fibroblast cells were used and the ODEs were numerically solved to predict the number of DSB complexes for doses in the range of 2-30 Gy and dose-rates in the range of 1-100 Gy/h. **Results:** Our computational analysis predicts that the number of DSB repair complexes formed in the high dose and high dose-rate limit can be several orders of magnitude higher than those in the low dose and low dose-rate limit. **Conclusions:** This work indicates that SBRT can lead to significantly higher therapeutic ratios in radiation therapy, if normal tissue toxicity can be maintained at levels comparable to those of conventional fractionation regimens. Since our computational analysis directly incorporates the quantification of cellular biochemical processes, its predictions are considerably more tractable in the high dose and high dose-rate regime than models such as the linear-quadratic model.

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