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We need to define safe levels of ionizing radiation exposure because of the high cost of medical technologies to cure disease. Estimating radiation dose is extremely challenging because it depends on the patient-specific dose distributions. Meanwhile, the number of exposed people is increasing. Here, we present a quantitative understanding of radiation dose-dependent genome instability in a single cell. We first define the dose response for two DSB repair pathways: NHEJ and HR. We then propose a stochastic model of NHEJ and HR dynamics to explain the dose response. We show that accumulated DSBs decrease the survival of cells and lead to cell death in a dose-dependent manner. The cell death kinetics follow a linear dose response at doses below a certain threshold. The model predicts that the number of potentially lethal DSBs in the absence of HR is not much different from that in the presence of HR. Since the number of potentially lethal DSBs is generally negligible under normal physiological doses, we propose that a cancer cell has to commit HR for a lethal event. We then show that the risk of cell death increases with dose and dose rate. Finally, we extend our model to propose a dose-dependent cell cycle dynamics in the presence of DNA damage and analyze the cell cycle phase distribution and duration of cells in each cell cycle stage. Our study may help a better understanding of radiation-induced genome instability./*

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