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Modeling the effects of G2-checkpoint dynamics on the low-dose hyper-radiosensitivity

In experimental studies, it has been found that certain cell lines are more sensitive to low-dose radiation than it is expected by the classical linear-quadratic model (LQ model). In fact, it is frequently observed that cells incur more damage at low doses than at higher dose. This effect has been termed hyper-radiosensitivity (HRS) and increased radio-resistance (IRR). The effect depends on the type of cells and on their phase in the cell cycle. In this talk, I will present the analysis of a differential equation model for the cell cycle that includes G2-checkpoint dynamics and radiation treatment. We fit the model to surviving fraction data for different cell lines including glioma cells, prostate cancer cells, as well as to cell populations that are enriched in certain cell-cycle phases. The HRS/IRR effect is measured in the literature through a ratio of the slope of the surviving curve at zero doses versus the slope of the corresponding LQ model. Using our model, we are able to derive an explicit formula for this ratio and we show that it corresponds very closely to experimental observations. Finally, we identify the dependence of this ratio on the surviving fraction at 2 Gy. It was speculated in the literature that such a relation exists. Our theoretical analysis will help to more systematically identify the HRS/IRR in cell lines and opens doors to analyzing its use in cancer treatment.

This is a joint work with Thomas Hillen and Gerda de Vries.