AbstractID: 12617 Title: Mechanistic model of radiation induced cancer after fractionated radiotherapy: fit to breast cancer risk after radiation therapy for Hodgkin's disease

Purpose: The strongly elevated risk of breast cancer after radiotherapy for Hodgkin's lymphoma has become a major concern for female survivors of this disease. The risk of breast cancer after Hodgkin's lymphoma has been mainly attributed to supradiaphragmatic radiotherapy. Women treated with mantle field radiation experience up to 30-fold increased risks for breast cancer compared with their peers in the general population. As a consequence radiation volumes and dose prescription for the treatment of Hodgkin's lymphoma have been reduced. The aim of this study is to develop a dose-response model for breast cancer using risk data from epidemiological studies Hodgkin's disease patients treated with radiation therapy. **Materials And Methods:** The linear-quadratic model of cell kill is applied to normal tissues which are unintentionally irradiated during a cancer treatment with radiotherapy. Tumor induction is modeled such that each transformation process results in a tumor cell. The microscopic transformation parameter was chosen such that in the limit of low dose and acute exposure the parameters of the linear-no-threshold model for tumor induction were approached. **Results:** The differential equations describing carcinoma and sarcoma induction were solved analytically. Cancer induction in this model is a function of treatment dose, the cell kill parameters (α, β), the tumor induction variable (μ) and the repopulation parameter (R). The dose-response relationship for breast cancer was derived based on (i) the cancer risk model described above, (i) the analysis of breast cancer induction after Hodgkin's disease, and (iii) the reconstruction of mantle field treatment plans for Hodgkin's patients treated with radiotherapy. The fitted model parameters for an $\alpha/\beta=3$ Gy were $\alpha=0.067Gy^{-1}$ and $R=0.62$. **Conclusions:** The developed model can be used to further optimize involved field radiotherapy for Hodgkin's lymphoma with regard to second cancer induction.