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Institutionen för Onkologi-patologi

Tumor radiosensitivity and proliferation as parameters for optimizing radiotherapy

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ABSTRACT

Radiotherapy is a widely used method to treat malignant tumors. However, the sensitivity to the treatment varies between tumors, and local tumor control is not always achieved. The balance between treatment success and the side effects of the treatment affords important information for developing treatment schedules at patient population level. Conversely there are no methods to tailor treatment schedules in an individual patient in clinical practice. The purpose of such methods would be to better balance treatment success with side effects in the individual, hopefully avoiding unnecessary treatments. As some tumors are resistant to radiotherapy doses that may be delivered without severe side effects, finding methods to sensitize tumor cells is of major importance.

In **Paper I** we evaluated a radiobiology model for predicting surviving fraction (SF) in five lung cancer cell lines. The purpose was to see whether it was important to include tumor cell proliferation during fractionated radiotherapy in a predicting radiobiology formula based on radiosensitivity, proliferation and number of tumor cells. When the clonogenic assay is used to establish SF, including proliferation seems to predict SF after fractionated radiation better than using inherent radiosensitivity alone.
In **Paper II** we evaluated the same radiobiology model in a clinical material of head and neck carcinomas. In 18 patients we compared using patient-specific radiobiological parameters with using population averages. Sensitivity in predicting local recurrence and predictive values were both better with individual parameters than with population averages. The accuracy of calculated probability of local control with the patient-specific-parameter model reached borderline statistical significance ($p = 0.07$).
In **Paper III** we investigated the entire material of head and neck carcinoma patients, including those receiving brachytherapy using a tumor control probability (TCP) model based on biologically effective dose (BED). Again we compared patient-specific radiobiological parameters with population averages to calculate individual TCPs. Evaluating the method using an ROC curve demonstrated a statistically significant difference in discriminating between local control or not when using patient specific parameters. This difference was not seen with population averages.
In **Paper IV**, the role of a phosphine gold(I) compound in altering radioresistance in a radioresistant human lung cancer cell line U1810 was investigated. This effect is achieved by shifting the intracellular redox balance by inhibiting TrxR. After a single fraction of clinically relevant radiation doses, a clear radio-sensitizing effect on SF and repopulation was demonstrated. Gene expression analysis demonstrated genetic expression changes in related cellular pathways connected to DNA repair, cellular response to stress, and cell cycle.

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