The effect of spatial and temporal dose distributions on radiation induced side effects in the lung

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ABSTRACT

In radiotherapy (RT), the aim is to kill all malignant cells in a tumor or to render them incapable of further division and multiplication without producing damage to the normal tissues surrounding the tumor. To achieve this, both the spatial and temporal distribution of dose delivery are important for optimizing the treatment. A sufficiently high dose must be delivered to the tumor cells and as low a dose as possible to normal tissues. The number of fractional doses delivered also impacts outcome due to the time-dependent repair of sublethal radiation damage, which differs in tumor and normal cells. In patients undergoing RT for tumors located in and near the thorax, irradiation of the healthy lung may induce radiation pneumonitis (RP), which can be a serious problem. Understanding the factors involved in the onset of RP is important for reducing its incidence

The overall aim of the thesis was to determine if radiation-induced side effects in lung can be modelled in terms of the spatial and temporal distributions of the doses delivered in conventional RT for breast cancer (BC) and hypofractionated stereotactic body radiotherapy (SBRT) for lung cancer.

Radiological changes in the lung were quantified with Computer Tomography (CT) after RT in 121 patients with breast cancer (BC). Their association with the spatial dose distribution as well as incidence of RP where studied. It was found that RP and radiological findings were associated with the spatial dose distribution. In a subgroup of 87 patients, data of the spatial dose distribution and incidence of RP were modelled using four different normal tissue complication probability (NTCP) models. The studied models fit quite accurately to data for the considered endpoints. Mean lung dose was shown to be a robust and simple parameter that correlated with the risk of RP.

The calculated spatial dose distribution in SBRT of tumors in the lungs, including breathing motions, were assessed for accuracy. The analysis showed that the dose in the central part of the gross tumor volume (GTV) was accurate to within 2–3% for commonly used algorithms; however in the lung tissue close to the GTV the different algorithms both over- and underestimates it, depending on type. When clinically relevant breathing motions were considered, the dose calculated for a static situation remained a relatively accurate estimate of the dose in the GTV. Data of dose distributions and incidence of RP after SBRT for lung cancer were fitted to a NTCP model in a cohort of 57 patients. Correction for fractionation was done in two ways: with the Linear-Quadratic (LQ) model and the Universal Survival Curve (USC). The modelling showed that low dose volumes contributes less to NTCP and high dose volumes comparatively more with the USC model, than the LQ model. The impact of fractionation in SBRT was analyzed using the LQ- and USC models for fractionation correction. The therapeutic window was shown to increase with number of fractions for a range of regimes (2 to 20 fractions) at target doses common in SBRT. Generally, a larger gain was predicted with the USC correction. At high doses per fraction, typical in SBRT, the USC model predicted a lower sensitivity for fractionation as compared to the LQ model.

In conclusion, the incidence of RP can be modelled, accounting for spatial and temporal dose distributions, especially in conventional RT of BC. In SBRT, with a more focused irradiation to very high doses, some uncertainties remain, both regarding the dependence of the spatial dose distribution and particularly of fractionation. The modelling shows that a less extreme hypo fractionation in SBRT may be a way to increase indications for SBRT. Generally, more data is needed for improved modelling.