Evaluation of dose-response models and parameters using clinical data from breast and lung cancer radiotherapy.

Ioannis Tsougos
Medical Physics Department, Medical School, University of Thessaly Larissa Hellas and Medical Radiation Physics, Karolinska Institutet,, Stockholm, Sweden.
[Fax: +30 2410670117, E-mail: jtsoug@med.uth.gr]
Thesis supervisor: Prof. C. Kappas
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A very important aspect in the optimization of radiation therapy is the adequate use of patient related information. Hence the description of the dependence of tumor and normal tissue responses on the irradiated volume and the dose-time-fractionation schedule should be introduced. In addition, the heterogeneity of the delivered dose distribution and tumor or normal tissue sensitivity variations as well as the inter patient radiosensitivity have to be taken into account clinically. Especially in the case of breast and lung cancer radiotherapy, recent developments have highlighted the importance of radiation lung toxicity and the occurrence of radiation pneumonitis, which can lead to severe respiratory dysfunction and even death, when combined with compromised lung function. Therefore in the present study, a treatment optimization procedure based on radiobiological modeling was used that considers the shape and the structure of the target tissues and healthy organs at risk, their relative position and their dose-response relations for the individual patient.

These mathematical models largely based on the Poisson statistics and the linear-quadratic model of cell kill, have been used to quantify the radiobiological response of normal human tissues and tumors to radiation therapy. The presented models predict a decreasing probability of achieving complication free tumor control with increasing tumor size and increasing volume of normal tissues irradiated. The radiobiological parameters of the examined cell survival and response models (e.g. α, β, D_{50}, γ, s) had to be estimated for certain normal tissues and tumors, and published parameters had to be examined in terms of their compatibility to certain treatment methodology and patient characteristics. The process for determining these dose-response relations was based on clinical materials where the treatment information and follow-up results of the individual patient were available. The statistical methods used, estimated and verified the parameters and their uncertainties.

Using this material, different methods of estimating the likelihood of radiation effects were evaluated. This was attempted by analyzing patient data based on their full dose distributions and associating the calculated complication rates with the clinical follow-up records. Additionally, the predictive strength of the radiobiological models, and the need for an update of the criteria that are being used in the current clinical practice were also examined.