Understanding tumour dynamics in vivo: The potential of kinetic models in radio-oncology

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Introduction

In vivo tumour response to ionizing radiation can differ remarkably from the response observed in vitro. This difference may be based on several processes related to the interaction of tumour cells with tumour environment. Also immune reactions and the related inflammatory processes may have an important influence. The adaption of radiobiological models based on the observation of clonogenic survival in vitro (e.g. the LQ model) to the situation in vivo is difficult. Repair, repopulation, interaction with host tissue, influence of radiotherapy onto vascularisation and oxygenation can be described by the rates of changes of the related quantities. This approach directly leads to kinetic models using differential equations. Probably, it may be difficult to solve the resulting differential equations analytically under certain conditions. This problem can be avoided by using numerical integration. We investigated a modified kinetic LQ model which has a high degree of flexibility for extensions and may therefore be a basis for better understanding of tumour dynamics in vivo.

Material and Methods

The proposed model is based on an ordinary differential equation for tumour population size, which is corresponding to the LQ-model. The LQ model leads to an insufficient description of the clonogenic survival for large fraction doses. Therefore, a kinetic sub-model for cellular repair was introduced. The coupling of the sub-model is performed by substituting the physical dose by a biological dose quantity, which is calculated by the sub-model. The resulting differential equations were implemented in a computer program using a Runge-Kutta algorithm. Also the kinetic model of Carlone et al. [1] was implemented. The surviving fractions as function of dose or time and the resulting TCP's for both models can be compared directly. Different therapy modalities were investigated. Also different approaches for repopulation were tested.

Results

For biologically targeted radionuclide therapy, the kinetic LQ-model is in agreement to classical LQ calculations [2]. For fractionated RT, the proposed model also is in agreement with the compartmental model of Carlone. Both models are fitting the linear-quadratic-linear behaviour, which can be observed for large fraction doses [3].

Conclusions

The kinetic formulation of the LQ-model offers a high degree of flexibility for extensions to repair, repopulation and different therapy modalities. In contrast to classical LQ models (and BED-calculations), the dynamics of a tumour can be studied easily. Therefore, the computer simulation also may be used for educational purpose (e.g. to learn about effects of hyper- or hypo-fractionation).

References

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