S. Becker, A. Mang, T.A. Schütz, A. Toma, T.M. Buzug
Institute of Medical Engineering, University of Lübeck, Germany
e-mail: {becker,buzug}@imt.uni-luebeck.de

A mathematical model of brain tumor and normal tissue responses to radiation therapy

The present work introduces a mathematical model that simulates the progression of malignant brain tumors as well as the effect of radiotherapy on cancerous and normal tissue. The spatio-temporal dynamics of a tumor cell density is described on the basis of a reaction-diffusion equation. In addition to passive diffusion and proliferation [1–3] this equation incorporates the effect of irradiation [2,3]. To account for the anisotropy of tumor diffusion within white matter, tensor information deduced from a probabilistic white matter atlas is incorporated into the model. The model also assumes logistic growth of the tumor cell population resulting in a lower net proliferation in regions of high cell density. The spatio-temporal effect of radiation is described by the linear-quadratic model.

In current mathematical models used to predict tumor growth and the biological effect of different treatment schedules, the mathematical description of radiation response in general is limited to cancerous cells. An optimization of treatment outcome, which includes a maximization of tumor control while minimizing normal tissue toxicity, however necessitates not only a quantification of the biological effect on cancerous tissue but also on healthy tissue. The present model therefore extends the standard approaches [2,3] by also modeling the effect of radiotherapy on normal tissue. A second differential equation describes the spatio-temporal progression of the necrotic density, incorporating the effects of irradiation on cancerous and normal tissue and a degradation due to phagocytosis. Furthermore, the tumor radiosensitivity is varied according to the local density of cancerous cells. This allows for indirectly considering the oxygenation and its influence on the radiosensitivity, as the growing tumor increases the lack of oxygen, which directly corresponds to the extent of radioresistance.

The numerical results show that the progression of primary brain tumors can plausibly be determined. The model is also used to quantitatively study the efficacy of irradiation under a variety of treatment schedules and dose distributions. The results illustrate the potential of the proposed model in finding a trade-off between tumor control and normal tissue toxicity. Incorporation into clinical planning systems could ultimately facilitate the administration of more appropriate, patient-specific treatment schedules and offers the promise of highly individualized radiation treatment for cancer patients. Avenues for future research include further clinical evaluations, incorporation of cell cycle dynamics and extension to other types of external beam radiation therapy.

References

[1] S. Becker and A. Mang and A. Toma and T.M. Buzug, *In-Silico Oncology: An Approximate Model of Brain Tumor Mass Effect based on Directly Manipulated Free Form Deformation*, 2010 Int J CARS **5**(5) 607–622.

[2] G. Powathil and M. Kohandel and S. Sivaloganathan and A. Oza and M. Milosevic, *Mathematical modeling of brain tumor: Effects of radiotherapy and chemotherapy*, 2007 Phys Med Biol **52** 3291–3306.

[3] R. Rockne and E.C. Alvord jr and J.K. Rockhill and K.R. Swanson, *A mathematical model for brain tumor response to radiation therapy*, 2009 J Math Biol **58** 561–578.