MULTI-SCALE MODELING OF CANCER PROGRESSION AND PREDICTION OF TUMOUR BEHAVIOUR BASED ON EXPERIMENTAL RESULTS

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Introduction

Colorectal carcinoma is acknowledged as the second leading cause of total cancer-related death in Europe. When a patient is diagnosed with colon cancer, liver is the most common site of metastatic lesions. The aim of this study was to numerically model the growth of the tumour and to predict the behaviour of cancer cells over time, taking into account the effects of prescribed drug therapy. The study enrolled a patient who suffered from inoperable liver metastatic disease. The real applied drug therapy data was incorporated in the model and the effect are introduced on both tumour and cellular level.

Methods

For the modelling of cancer progression a model of spatial-temporal changes of cell concentration proposed by Swanson *et al* [Swanson, 2003] was used. The basic equation is given by:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial \mathbf{x}^2} + \rho c - F(t)c \qquad (1)$$

where D is the diffusion coefficient, ρ is the proliferation rate of cells, and $F(t)$ is the external effect of applied drug therapy.

The effect of drug therapy is also modelled on cellular level, since the applied therapy is influencing the EGFR signalling pathway, as explained in [Tang, 2012]. The proliferation rate is decaying with the increase of drug concentration, and this was modelled using a Hill function.

Results and discussion

The study data comprised of CT scan examinations scheduled averagely every 67 days from the beginning of the treatment. Drug therapy included chimeric anti-EGFR monoclonal antibody agent combined with four other chemotherapeutics. Imaging analysis was performed on CT scan images, to obtain both the initial configuration and tumour volumes in specific moments in time. This data was further used to determine the unknown parameters of the model (D and ρ).

Figure 1 shows the diagram of variation of tumour volume over time. Above the diagram states of tumour (finite element models) in specific moments in time are shown. As it can be seen, the experimental and predicted curves agree very well and that demonstrates that this numerical model can be successfully used to predict tumour behaviour.

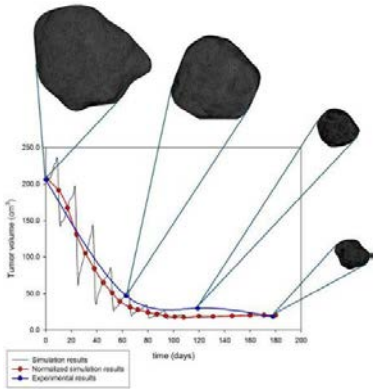

Figure 1: Prediction of behaviour of tumour with effect of drug therapy taken into account. Black line – prediction obtained using numerical modeling; red line - normalized simulation results; blue line - experimental results obtained from patient screening

References

Swanson, K. R. et al, Virtual and real brain tumors: using mathematical modeling to quantify glioma growth and invasion, J. Neurol. Sci., 216: 1-10, 2003.

Tang, L., Su, J., Huang, D-S., Lee, D.Y., Li, K.C., Zhoul, X., An integrated multiscale mechanistic model for cancer drug therapy, ISRN Biomathematics, vol. 2012, article ID 818492, 12 pages, 2012., doi:10.5402/2012/818492