

MECHANICALLY COUPLED REACTION-DIFFUSION MODEL OF MACROSCOPIC BRAIN TUMOUR GROWTH

Daniel Abler (1), Philippe Büchler (1)

1. Institute for Surgical Technology & Biomechanics, University of Bern, Switzerland

Introduction

Brain tumours represent a rare but serious medical condition, with glioblastoma multiforme (GBM) being the most frequent malignant histological type. These tumours are characterized by invasive growth, infiltrating surrounding healthy tissue, and poor long term prognosis with 5-y survival rates below 3% [1]. Growth and dynamics of brain tumours, and GBM in particular, have been studied extensively by means of different computational modelling approaches. Most macroscopic models of spatial tumour evolution within a patient-specific anatomy have been based either on reaction-diffusion models, e.g. [2], accounting for the invasive growth of GBM, or on purely mechanical models, e.g. [3], simulating the mass-effect caused by a growing solid tumour. Few models, such as [4, 5], consider both effects in a single 3D model in order to better understand disease progression and to support personalized treatments.

Methods

We use the finite element method (FEM) for simulating the invasion of GBM into brain tissue and the mechanical interaction between tumour and healthy tissue components. The process of proliferation and invasion is modelled as a reaction-diffusion equation, while the simulation of the mechanic interaction relies on a linear-elastic material model. Both are coupled by relating local increase in tumour cell concentration to the generation of isotropic strain in the corresponding tissue volume element. Implementation is based on the heat transfer and thermal expansion module in Abaqus (Simulia). The simulation accounts for multiple brain regions with values for proliferation, isotropic diffusion and mechanical properties derived from literature. An automatic pre-processing pipeline (C++ with VTK, CGAL) has been developed for creating tetrahedral FEM meshes from patient image segmentations, including assignment of suitable material properties and boundary conditions to the different regions of interest.

Results

In combination with image segmentation tools, the pre-processing pipeline permits rapid generation of patient-specific anatomical FEM models for personalized simulations, Fig. 1.

Tumours have been seeded at different locations in FEM models derived from publicly available human brain atlases. Their growth pattern has been studied in function of seed location.

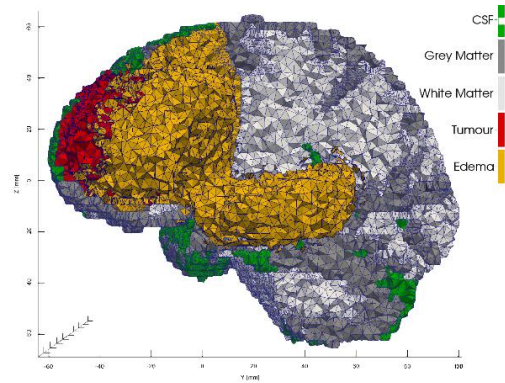


Figure 1: Tetrahedral mesh distinguishing several healthy-brain and tumour regions; generated from patient data using pre-processing pipeline.

Discussion

This study reports first results of the evaluation of a personalizable model of GBM growth. The relative magnitude of diffusion versus the strength of mechanical coupling in this model represents the tumour's propensity for healthy tissue invasion or solid tumour formation, respectively. The model predicts non-isotropic growth patterns, similar to those observed in clinical cases. However, further attention needs to be directed to quantitative validation of model predictions, for example against longitudinal imaging data. In particular, calibration and validation of the mechanical coupling term and its dependence on tumour type are less studied in literature. Such investigation may require multiple improvements upon the presented model and implementation, e.g. adoption of a non-lagrangian formulation to support large tissue deformations, a more appropriate constitutive model for brain tissue, or the use of personalized model parametrizations.

References

1. Ohgaki and Kleihues, Acta Neuropathol, 109:93-108, 2005.
2. Swanson et al., J. Neurol. Sci., 216 (1):1-10, 2003.
3. Hogeia et al., Phys. Med. Biol., 52 (23):6893-6908, 2007.
4. Clatz et al., IEEE Trans. Med. Imag., 24 (10):1334-1346, 2005.
5. Hogeia et al., SIAM J. Sci. Comput., 30 (6):3050-3072, 2008.

Acknowledgements

The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 600841.