Congrès des Jeunes Chercheurs en Mathématiques Appliquées - Modèle de résumé

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Biographie – I have an engineer degree from Ecole Centrale de Nantes in Applied Mathematics and Biology. My PhD is the meeting point between knowledge in applied mathematics and the future of patients diagnosed with severe brain cancer: Glioblastoma Multiforme. The PhD started in November 2019 and is fully financed with a scholarship from the Ministère de la recherche.

Resumé :

Glioblastoma Multiforme (GBM) is the deadliest and most frequent brain tumour. Despite the research of new treatments, patients still show poor prognosis in the long run: only 5% of patients survive 5 years post-prognosis.

Usually, patients undergo emergency surgery (if the surgery is possible), then the treatment consists in radiotherapy plus concomitant and adjuvant Temozolomide (TMZ) therapy [6]. More efficient therapies remain a major preoccupation to cure GBM, among them, immunotherapies is more and more a subject of research for gliomas and could improve the current prognosis of GBM patients.

When a patient gets diagnosed with GBM, tumour cells have already achieved enough tumour promotion mechanisms in order to evade the immune system and to proliferate in the brain. In that sense, we chose to model the GBM growth based on the process of tumour associated angiogenesis.

Angiogenesis is the ensemble of phenomenon that allow the formation of new blood vessels from pre-existing blood vessels. Those physiological processes happen not only for cancer patients, but tumours have the ability to use angiogenesis in their favor as a tumour promoter. Tumour cells rely on nutrients and O_2 for their growth, provided by blood vessels. During tumour growth, the tumour core lacks O_2 inducing hypoxia in the tumour core. Hypoxia prevents most tumour cellular activities, acting like a tumour suppressor process. To fight hypoxia, hypoxic tumour cells produce proangiogenic factors such as Vascular Endothelial Growth Factors (VEGF), that are the main factors produced in GBM. Proangiogenic factors promote angiogenesis meaning that more blood vessels are produced, and so more nutrients and O_2 are provided to the tumour cells. Angiogenesis mathematical models have already been developed: using PDEs [3], some adding stochastic parts in the modeling [7], or working at a mesoscopic scale [1].

However in this work, we consider more realistic situation to the tumour associated angiogenesis model by working on Magnetic Resonance Imaging (MRIs) data based on a real patient and by modeling the behaviour of GBM growth through the treatments usually administered to patients. Indeed MRIs are required to certify the diagnosis of GBM, and it is easier nowadays to get information from MRI as some deep learning techniques can be used to extract medical data. With numerical tools, it is possible to perform segmentation of GBM tumours based on MRI. Recent studies show also that information on the tumour cells behaviour can be acquired with immunohistochemistry data, for example by identifying GBM subtypes [2] but we will not consider those different subtypes in this work.

This results in a homogeneous zero-flux boundary conditions nonlinear system with 4 equations and 4 unknowns: the density of tumour cells (u), the O2 concentration (c), the density of endothelial cells (u_e) and the vascular endothelial growth factor concentration (v)

$$\partial_t u - \nabla \cdot (\Lambda_1(x)(a(u)\nabla u - \chi_1(u)\nabla c)) = \rho_1 h(c) f_{u_T}(u) - \beta_1 u - T_{treat}(t,u), \tag{1a}$$
$$\partial_t c - \nabla \cdot (D_2 \nabla c) = \alpha_2 u_e - \beta_2 c - \gamma_2 uc, \tag{1b}$$
$$\partial_t u_e - \nabla \cdot (\Lambda_3(x)(a(u_e)\nabla u_e - \chi_3(u_e)\nabla v)) = \rho_3 f_{u_T}(u_e) - \beta_3 u_e, \tag{1c}$$
$$\partial_t v - \nabla \cdot (D_4 \nabla v) = \alpha_4 g(c) u - \beta_4 v - \gamma_4 u_e v. \tag{1d}$$

Working on MRI is numerically challenging because on real MRI we can not have constrained mesh to solve our equations on. Finite volume scheme based on TPFA (Two Point Flux Approximation) can not ensure the positivity of numerical solutions. It is then needed to use more sophisticated numerical schemes in order to ensure the positivity of the solutions. Our approach is based on a CVFE (Control Volume Finite Element) scheme in which nonlinear numerical Gudonov fluxes are used to ensure the positivity.

Using real patient data, it is interesting in the long run to include the treatments in the model to be able to match data and simulations. Currently patients with GBM are treated using surgery, chemotherapy with TMZ and radiotherapy, we will only consider those treatments in our model. Chemotherapy and surgery were first used in PDEs model around gliomas but more robust models have been developed: on chemotherapy with hypoxic cells [5], on surgery and radiotherapy with an haptotaxis model [4] and even on immunotherapy in gliomas [8]. Choosing to model those treatments will allow us to compare their impact on the GBM growth through the recovery of a patient, and so, analyse their advantages and drawbacks on the tumour cells.

Numerical simulations obtained are available following this link `https://www.youtube.com/watch?v=vJkMJ5bNoWA`. The work related here is going under the publishing process.

Références

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