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COMPUTATIONAL MODEL OF THE MASS TRANSPORT IN A TUMOR NODULE DURING INTRAPERITONEAL CHEMOTHERAPY

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INTRODUCTION

Carcinomatosis is characterized by a widespread growth of tumor nodules in the peritoneal cavity. Patients with peritoneal carcinomatosis cannot be adequately treated by intravenous chemotherapy. The intraperitoneal administration of chemotherapy is an alternative treatment, allowing for higher local intratumor concentrations of the cytotoxic agent compared to intravenous administration [1]. Although this therapy appears promising, its actual application is still limited due to the poor drug penetration (only a few millimeters) in the tumor. It is thus essential to gain more insight into the parameters that influence the drug transport via the intraperitoneal route. Therefore, we developed a CFD (computational fluid dynamics) model that incorporates both diffusive and convective drug transport in a simplified configuration of a tumor nodule.

METHODS

A 3D geometry was created, consisting of a single tumor nodule and a simplified vascular network (Fig. 1). Subsequently, the volumes were meshed in $\pm 2 \cdot 10^6$ tetrahedral elements. The tumor tissue was modeled as an isotropic porous medium. A fixed mass fraction of the cytotoxic agent was specified at the border of the tumor tissue. The boundary conditions of the vascular network were set to an inflow velocity of 1 mm/s and a pressure of 0 Pa at the outflow. The CFD model was solved by transient simulations (150 time steps of 10s). A parameter study was performed in order to study the impact of the drug diffusivity ($9 \cdot 10^{-9}$, $9 \cdot 10^{-10}$ and $9 \cdot 10^{-11}$ m^2/s), the permeability of the porous tumor tissue (10^{-14} and 10^{-13} m^2) and the drug concentration (mass fraction of 10% and 20% at the tumor edge).

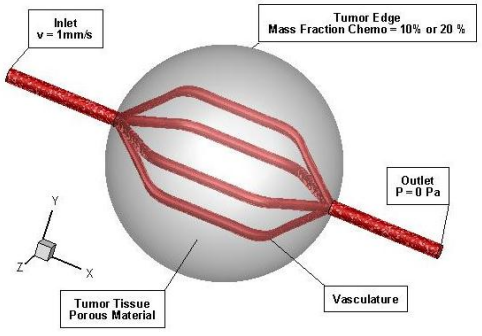

Figure 1: Visualization of the model geometry showing the tumor tissue, its vasculature and the applied boundary conditions

RESULTS

For all simulations, the molecular concentration was monitored at the vascular outlet for each time step. When all other parameters were kept constant, a clear increase in the molar concentration of chemo at the vascular outlet was noted with increasing drug diffusivity (Fig. 2 left and Fig. 3). The same effect, although smaller, could be noted for the increase in the applied mass fraction at the tumor edge (Fig. 2, right).

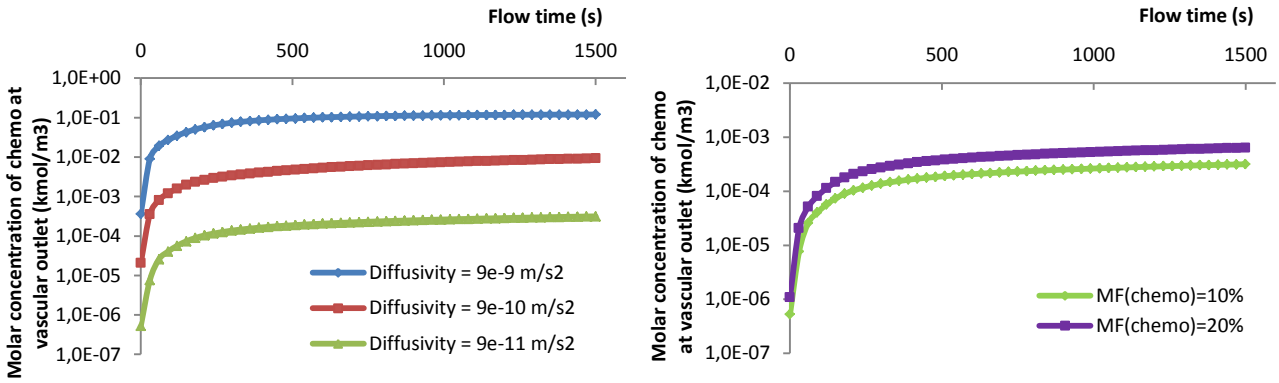

Figure 2: Left: Comparison of chemo concentration at vascular outlet for varying drug diffusivities. Right: Comparison of chemo concentration at vascular outlet for different mass fractions of chemo applied at the tumor edge.

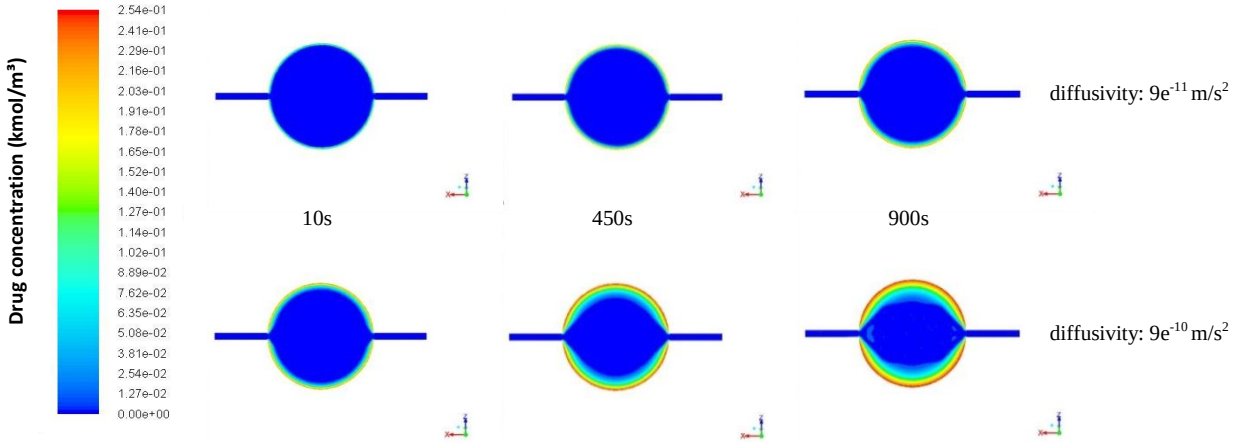

Figure 2: Concentration profiles (kmol/m^3) in plane perpendicular to z-axis for a flow time of 10, 450 and 900 seconds. Top row: drug diffusivity of 9e^{-11}m/s^2. Bottom row: drug diffusivity of 9e^{-10}m/s^2.

When only the permeability of the porous medium was changed, there was a slight increase in the outlet concentration of chemotherapy (in the order of 1e^{-6} kmol/m^3). The effect of changes in this parameter appeared to be a lot smaller compared to the other parameters.

CONCLUSION

Initial results with the developed model indicate that the model is able to simulate the relative impact of different drug and tissue properties on the drug transport within a tumor nodule during peritoneal chemotherapy. Future work will focus on extending the model to more realistic configurations and in vitro and in vivo validation.

REFERENCES

[1] Ceelen, W.P., Flessner, M.F. Intraperitoneal therapy for peritoneal tumors: biophysics and clinical evidence. Nature Reviews Clinical Oncology 2010; 7:108-115