

# Modeling the drug transport in a single tumor nodule during intraperitoneal chemotherapy

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## Introduction

Intraperitoneal (IP) chemotherapy is fundamentally different from conventional intravenous chemotherapy, since tumor nodules are brought into direct contact with the cytotoxic drug solution instead of convective drug transport through the circulation. The aim of IP chemotherapy is to increase the intratumorous drug concentration, while limiting the systemic drug dose and undesired side effects. IP therapy is mainly used to treat patients with peritoneal carcinomatosis, i.e. a wide-spread growth of tumor nodules on the peritoneal membrane which is often a metastatic disease with a poor survival prognosis. Although IP chemotherapy is a promising technique<sup>[1]</sup>, the current drawback is the limited drug penetration depth in the tumor tissue. Therefore, we studied the impact of a number of parameters on the transport of a cytotoxic drug in a single tumor nodule using a porous medium modeling approach.

## Methods

A 3D computational fluid dynamics (CFD) model of a single tumor nodule and its simplified vascular network (Figure 1) was created. To model the tissue, an isotropic porous medium model was used and the vasculature was modeled as a fluid domain. A parameter study was performed in which the drug diffusivity ( $9 \cdot 10^{-9}$ ,  $9 \cdot 10^{-10}$  and  $9 \cdot 10^{-11}$  m<sup>2</sup>/s), tissue permeability ( $10^{-14}$  and  $10^{-13}$  m<sup>2</sup>) and mass fraction of chemo at the tumor edge (10% and 20%) were varied.

## Results

The results of the parameter study showed different effects on local and systemic concentrations. Increasing the mass fraction from for 10% to 20%, for example, lead to a doubling ( $3 \cdot 10^{-4}$  to  $6 \cdot 10^{-4}$  kmol/m<sup>3</sup> after 1500 s of therapy) (Figure 2a) of the systemic concentration, but only a very limited increase in penetration depth of the drug in the tissue (Figure 2b). Increasing the drug diffusivity from  $9 \cdot 10^{-9}$  to  $9 \cdot 10^{-10}$  m<sup>2</sup>/s on the other hand resulted in an increase in both local penetration and systemic concentrations (an added 5 mm of penetration depth for an increase from  $3,2 \cdot 10^{-4}$  to  $9,3 \cdot 10^{-3}$  kmol/m<sup>3</sup> after 1500 s of therapy). Increasing the tissue permeability resulted in higher systemic concentrations of chemo and a minor increase in penetration depth, but the response to permeability changes was found to be strongly non-linear.

## Conclusion

Initial results indicate that the model is able to simulate the impact of different drug and tissue properties on both the local and systemic drug concentration. Future work will focus on extending the model to more realistic configurations (e.g. by taking into account interstitial fluid pressures) and validation of the parameters.

## 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

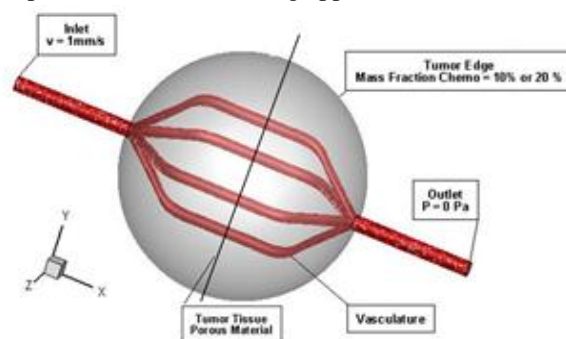


Figure 1: Visualization of the model geometry showing the tumor tissue, its vasculature and the applied boundary conditions

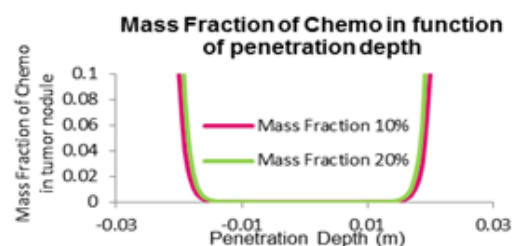


Figure 2: (a) Mass fraction of chemo in function of penetration depth

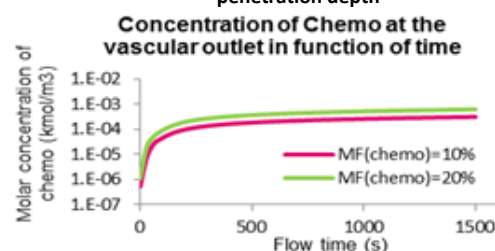


Figure 2: (b) Systemic concentration of chemo in function of time