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Pore-scale analysis of fluid transport in different grades of brain tumours considering the effect of extracellular matrix

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Glioblastoma (GBM), one of the most common aggressive brain tumours, accounts for more than 50% of primary malignant central nervous system (CNS) gliomas in adults. According to the World Health Organization (WHO) classification [1], brain tumours can be graded from 1 to 4 as pilocytic astrocytoma (PA), diffuse astrocytoma (DA), anaplastic astrocytoma (AA) and GBM in terms of malignancy and abnormality. GBM remains challenging to treat with a high 5-year modality rate of more than 90%. This undesirable efficacy can be partially attributed to the higher levels of the extracellular matrix (ECM), thereby leading to disappointing drug delivery outcomes. Hyaluronic acid (HA), one of the major components of ECM, is 8 times and even higher in GBM than the HA level in brain normal tissue, However, how HA affects the ISF transport in the microscale channels is insufficiently understood.
In this study, we first reconstructed the different 3D tumour microstructures from Grade 1 to 4 based on the microscopic morphology of U87 cell lines and their geometrical information (porosity and cell size) [2]. We conducted the simulations using the open-source computational fluid dynamics software OpenFOAM [3]. We confirmed the representative element volume (REV) size (200 μm) and validated simulation results with the reported experimental results [4]. We then quantified the relationship between tissue hydraulic permeability and HA concentration in the low- and high-grade tumours. Specifically, we indicated that the average permeability between PA and DA decreases by 23.5% with an average 21.6% increase of porosity and the same level of HA deposition. While the average porosity increased by 33% from the low-grade to the high-grade tumours, the mean hydraulic permeability decreased by 23.8% with the 2.7 times increase in the HA concentration range. We identified the necrotic region (NR) in GBM as more permeable than high-grade tumours, due to the highest porosity and relatively lower HA concentrations. Therefore, results from our computational models underscore the dominant effect of the HA matrix when simulating the ISF flow in brain tumours. Finally, we established a significant correlation between hydraulic permeability and HA concentration range in different grades of brain tumours, and also found that low- and high-grade tumour tissues are more permeable than brain normal tissues [5].
In this work, we developed a modelling framework to investigate the ISF transport in different WHO Grades of brain tumours. We also linked the ECM permeability to ISF flow through the extracellular space on the pore scale. The findings from this work can advance the accuracy of prediction of fluid transport properties in the brain tumour, and hence also the efficiency of potential drug delivery strategies for brain tumours and other disorders.

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