Interstitial Fluid Pressure and Hydraulic Conductivity in Solid Tumors: Introducing an In-Vitro Method for Measuring the Hydraulic Conductivity of Tumor Tissue

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Introduction

Resistance against drug delivery is a challenge in oncology, preventing the development of optimal therapeutic outcomes. This has been related to a group of hostile biophysical characteristics in the tumor microenvironment. Among them, the elevated interstitial fluid pressure (IFP) in solid tumors has been identified as a barrier for drug transport. Also, the hydraulic conductivity (K) of tumor stroma strongly correlates with the IFP. However, values of K in human cancer tissues are quite limited. Here, we developed a novel in vitro setup that allows to measure K in clinical samples. Moreover, the dependency of IFP over K was investigated via a numerical method.

Methods

We developed an apparatus based on modified Ussing diffusion chambers. The setup comprises the diffusion chambers along with a bubble tracker device as an index for quantifying the amount of fluid exchange through the tissue due to a hydrostatic pressure gradient in a closed system. The rate of bubble movements was converted into K values by accounting for several parameters such as the sample thickness, buffer solution viscosity, and the pressure magnitude. Also, a 2D computational fluid dynamics (CFD) model was used to simulate the sensitivity of the IFP profile to the magnitude of K.

Results

The measured values (K ranging between $6.8\text{E-}16$ and $4.1\text{E-}14$ $\text{m}^2/\text{Pa}\cdot\text{s}$) demonstrated a good agreement with previously published values, which were either measured in animal studies or estimated indirectly. The results indicated heterogeneity of hydraulic conductivity values in a single tumor up to a factor of 4.3. Moreover, results demonstrated that K values for the same tumor type can vary significantly. The CFD model showed that changes in K may significantly affect the tumor IFP depending on the tumor size and shape.

Conclusion

We successfully built a setup that allows to measure the hydraulic conductivity of human cancer tissue samples. Regarding the relatively high sensitivity of IFP to K values, these results can inform novel therapeutic approaches that target the biomechanical tumor environment.