Introduction

Convection-enhanced delivery (CED) is a surgical technique, used with invasive brain tumours, that consists in injecting, directly into the parenchyma, therapeutics. Predicting their distribution inside the tumour is crucial to optimize the infusion point and the flow rate. Indeed, the parenchyma can be considered as a porous media with the neurons immersed in the interstitial fluid. However, the relationship between the axons geometry and the convective part of the flux, which drives the drug through the brain, is currently unclear. In order to shed light on this particular aspect of CED, this paper proposes a numerical method to compute the hydraulic permeability starting from axons electron microscopy (EM) images.

Methods

The EM images where acquired from data provided by [1] and obtained for a monkey brain in the corpus callosum (CC) and superior fascicle (SF). Manual segmentation separated the axons from the extracellular matrix and the interstitial fluid. Then, they were imported in the finite element software ANSYS to compute velocity and pressure fields of the fluid moving through the pores. Since in CED intervention the flow rate is very low, in first approximation we can neglect the tissue deformation and therefore model the axons as rigid. This procedure evaluates the permeability (k) by means of Darcy's law:

$$v = \frac{k}{\mu}\nabla p,$$

With:

- v averaged velocity of the fluid in the porous medium
- μ viscosity
- ∇p pressure loss across the volume.

Results

Fig-1-A shows segmented samples, while in Fig-1-B it is shown how increasing the size of the Representative Volume Element (RVE) considered, a better estimate of the permeability is obtained for both SF and CC. To avoid possible errors due to edge effects and boundary conditions, RVEs of 10 (SF) and 12 µm (CC) representative length were used to obtain the permeability values reported in Fig-1-C.

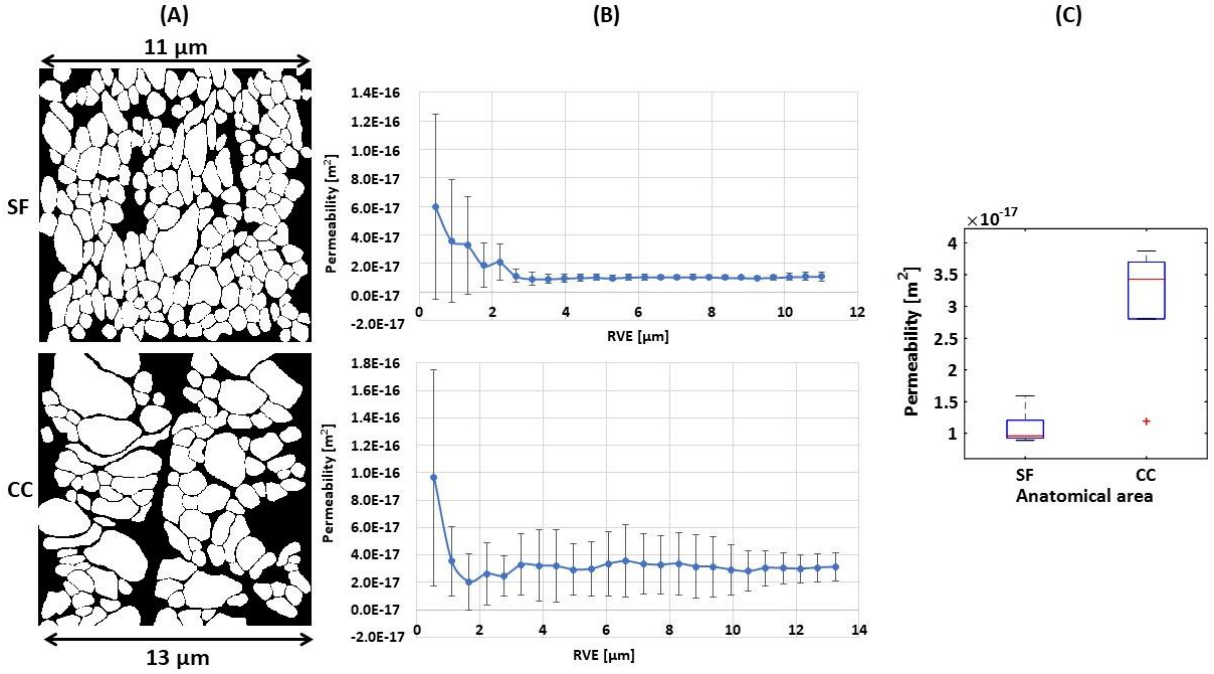

Fig-1: (A) Manual segmentation: axons (white), interstitial fluid (black). (B) Permeability as a function of the RVE size. (C) SF and CC permeability boxplot for RVEs of 10 and 12 µm respectively.

Discussion

In this study, we have shown the feasibility of using a numerical method to compute the hydraulic permeability in the brain with results in very good agreement with experimental data found in literature [2]. This work can be considered as a first step towards a more comprehensive understanding of how the drug delivery depends on the micro-structure. [1][2][3][4][5]

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