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ORIGINAL PAPER

2D Finite Element Analysis Of Cerebral Tissue Swelling Occurrence in Brain Ischaemia-Reperfusion Injury

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ABSTRACT

Brain vasogenic oedema is an injury that can occur after reperfusion treatment of cerebral ischaemic stroke patient. It can lead to brain tissue swelling, which can cause brain herniation that may affect brain function. A mathematical model describing this injury has been developed using capillary filtration and poroelastic theory to represent oedema formation and brain tissue swelling, respectively. In this paper, a preliminary 2D representation of human brain is developed and the mathematical model of ischaemia-reperfusion injury is then solved using finite element method. The size and location of the ischaemic stroke infarct are varied and the movement of the midline that divides the cerebrals is observed. Results show that herniation level is worsened especially for large infarct size and for infarct that is closer to the brain ventricle. Further validation of the model using MRI data and patient-specific representation is needed to estimate the brain swelling and treatment planning.

INTRODUCTION

Brain oedema formation due to cerebral ischaemia-reperfusion injury can be observed using medical imaging modalities such as CT and MRI scans by the formation of brain midline structure displacement or brain herniation [1] or by brain tissue swelling [2]. The herniation usually results in the compression of brain ventricle and cerebral microvessels, which further results in the occurrence of secondary ischaemia [3]. The presence of herniation may indicate the rise in the intracranial pressure (ICP) and it may cause permanent neurological problems and even fatality [4]. Several treatments are available for brain oedema such as decompressive surgery and osmotherapy, although the effectiveness of these treatments remains questionable [5, 6] due to the complicated nature of oedema formation.

A mathematical model has been developed to further understand the formation of brain tissue swelling due to BBB breakdown using poroelastic theory, which was initially used to study soil mechanics [7] and has been extensively used to study the mechanics of the brain [8-10]. In this theory, the brain tissue is assumed to be homogeneous, has linear elastic property, and contain water and blood in a porous structure. A comprehensive mathematical framework of this theory can be found in [11].

In this paper, the brain tissue swelling after a cerebral ischaemia-reperfusion injury is investigated using finite element analysis in a simplified 2D model of the brain. The objective is to observe the effect of infarct size and location to the formation of brain herniation. This will be a preliminary study before a more complete validation using MRI data of ischaemic stroke patient can be done.

MATERIALS AND METHOD

Theory

During ischaemic stroke, the lack of oxygen and nutrient to the affected region creates a series of biochemical reactions that destroys the endothelial cells surrounding the cerebral microvessels leading to the blood-brain barrier (BBB) breakdown, which increases the BBB permeability [12]. When blood flow is restored after reperfusion treatment, ions and some protein plasma can filtrate through the damaged BBB creating osmotic pressure difference between the capillary and interstitial space. This can cause the flux of water from the capillary and accumulate in the tissue space and causes the formation of vasogenic oedema, eventually leading to the formation of cerebral tissue swelling. Figure 1 illustrates the process of water accumulation into the interstitial space after BBB breakdown

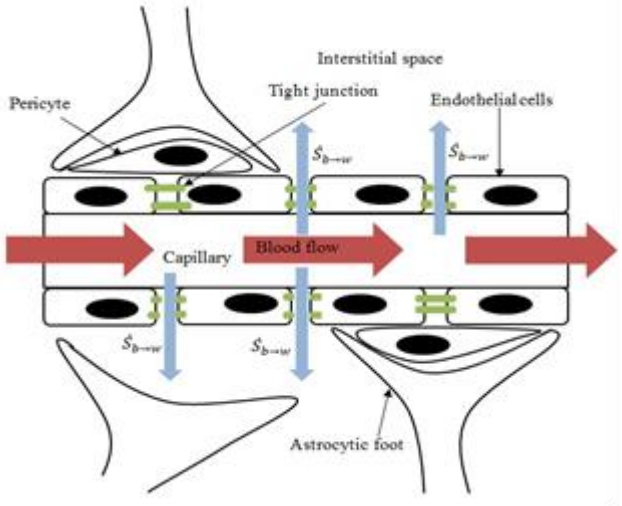

Fig. 1 Flux of water after BBB breakdown. $Sb \rightarrow w$ represents the water movement from blood capillaries into the cerebral tissues via capillary filtration.

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Mathematical Model

The formation of cerebral tissue swelling due to capillary filtration has been modeled by [11] using capillary filtration model and poroelastic theory. The governing equations are given as:

$$\nabla \cdot \sigma_{ij} - \alpha_w \nabla P_w = 0 \quad (1)$$

$$1 \partial P_w / Q_w \partial t - k_w \nabla^2 P_w - S_{b \to w} = 0 \quad (2)$$

where σ_{ij} is the total stress of the tissue, P_w is the interstitial water pressure, α_w is the Biot parameter for water, Q_w is the relative compressibility of water, $k_w (= \kappa w / \mu w)$ is the permeability of water, t is time.

The term $S_{b \to w}$ represents the water transfer from the capillary space into the cerebral interstitial space via capillary filtration and is given by:

$$S_{b \to w} = 2 \bar{n}_b L_p / (f [(P_b - P_w) - \sigma \Pi_b]) \quad (3)$$

where $\bar{n}_b$ is the baseline volume fraction of the blood, L_p is the hydraulic permeability of the capillary, R_c is the baseline value of capillary radius, σ is the reflection coefficient, Π_b is the osmotic pressure in the capillary and P_b is the blood pressure, which has been assumed constant. Lastly, the term f represents the fraction of vessels that remain open after the reperfusion and swelling process at each point in space and time, and this can be modelled using a heaviside function.

The total stress, σ_{ij}, is linearly related to the strain, ε_{ij}, using typical linear elasticity relation [13].

$$\sigma_{ij} = 2G\varepsilon_{ij} + (2Gv1/2v)\varepsilon_{ii} \quad (4)$$

where G, and v are the shear modulus and Poisson's ratio of the cerebral tissue, respectively.

The boundary conditions at the skull and the ventricle are set as stationary and pressure at baseline ICP, P = 1330 Pa. The tissue is assume to initially static and the fluid pressure is at the baseline ICP. The simulations are solved using open-source finite element analysis software ELMER and are analysed using ParaView. The list of parameters value can be found in [11].

RESULTS AND DISCUSSION

Simulation results

The capillary filtration was simulated for simulation time until 1 hour. Figure 2 shows the cerebral interstitial pressure and tissue displacement for various infarct sizes located near the brain ventricle. The tissue displacement starts to develop at the outermost radius of the infarct before slowly spreading to the inside and outside of the infarct. Meanwhile, the pressure starts to rise within the center of the core and then spreads in the direction of the infarct radius.

However, due to the boundary conditions imposed at the subarachnoid and ventricular layers, the displacement and pressure gradually decrease near these layers. The tissue displacement pushes the other side of the cerebral tissue as indicated by the deformation of the middle line to the right side. The deformation of this line increases as the size of the infarct becomes larger.

Effect of infarct size and location on brain herniation

The changes in maximum displacement and maximum pressure when the infarct distance from the ventricle is varied are shown in **Figure 3**. The maximum displacement increases when the distance from the ventricle increases except for the case of the infarct radius at 7 mm. For this infarct size, there is a slight drop in the maximum displacement for the infarct distance from 7 mm to 21 mm and the infarct distance from 42 mm to 49 mm. Meanwhile, for the maximum pressure, there is no substantial difference when the distance is varied with the exception of the case for a 7 mm infarct radius, although the difference for this case is only about 25 Pa from the other cases. This difference is due to the 'edge effect', in which the infarct is located near the subarachnoid and ventricle layer that have constant displacement and pressure values. In reality, the ventricle does not have a fixed shape and position but it may move and be compressed during brain tissue swelling. The compression of the ventricle is also a good indicator of cerebral swelling in CT images [14]. It is known that the existence of AQP4 at the interface of the

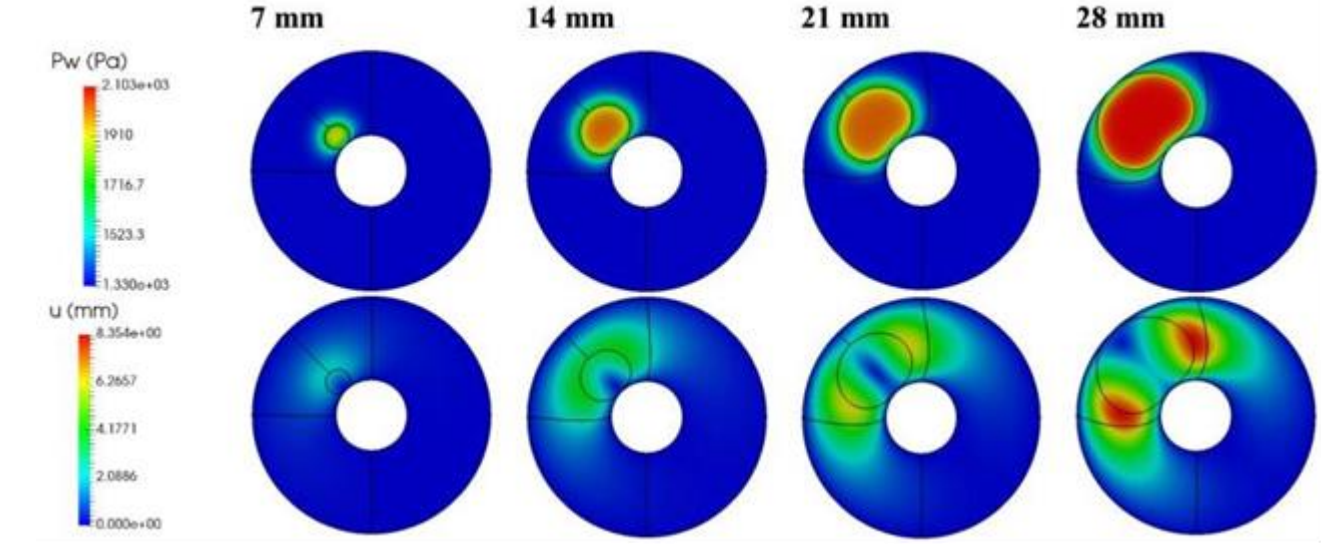

Fig. 2 2D simulation results for various infarct sizes. (Top) Interstitial pressure. (Bottom) Tissue displacement.

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ventricle and the cerebral space can help in the clearance of oedematous fluid [15]. Thus, a further improvement to the model could be made by incorporating a pressure gradient [8] and stress-free boundary conditions [16] at the ventricle to see how the presence of this fluid cavity affects the progression of cerebral swelling and fluid pressure development. However, for the sake of model simplification, this assumption is applied here.

Future Works

It has been assumed in this study that the cerebral tissue property is homogeneous throughout the geometry. In reality, the cerebral tissue material properties are different for those located in the white and grey matter of the cerebral space. Oedema is less likely to develop in the grey matter area due to its twisted structure and it has a low tissue compliance as compared to white matter [2]. The study done by Smillie, Sobey [17] also assumed that the mechanical properties of white and grey matter are the same due to the lack of data available. However, they use different fluid permeability values within these two cerebral structures.

Meanwhile, the model developed by Nagashima, Shirakuni [18] used two different cerebral tissue hydraulic conductivity values to account for their different properties. Therefore, incorporating the different mechanical properties of the brain tissues in the model could improve the brain tissue swelling prediction.

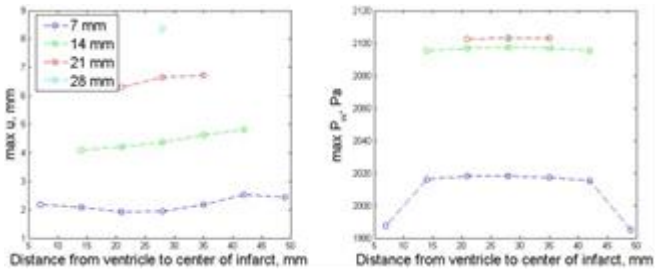

Fig. 3 Variation of the maximum brain tissue displacement and interstitial pressure with the infarct size and distance from the ventricle.

Another aspect worth studying is the vasogenic oedema resolution. The oedematous fluid will move out into the ventricles and subarachnoid spaces via glia limitans, into the capillary endothelium via the astrocytic foot or by metabolic degradation [19, 20]. The presence of aquaporin-4 (AQP4) channels in the glia limitans and astrocytic foot [20] facilitate the removal of the oedematous fluid. However, AQP4 also plays a role in the formation of cytotoxic oedema that causes intracellular swelling, which does not result in an increase in ICP and brain tissue swelling [4]. The function of AQP4 has been demonstrated by using a mathematical model [21]. Modification of the current model through the inclusion of the role of AQP4 might provide new insight towards the occurrence of reperfusion injury.

CONCLUSION

From this study, it was found that the size and location of cerebral ischaemic infarct can affect the degree of brain herniation. This is shown by the deflection of the midline that divides the two cerebrals. In addition, the maximum brain tissue displacement and interstitial pressure are increase as the infarct sizes increase. These findings indicate that ischaemic infarct size plays an important role in determining the severity of brain tissue swelling.

The results obtained here provide further useful information such as: (1) the importance of making the ventricle structure movable for better quantification of the brain tissue swelling; and (2) confirms the occurrence of herniation during brain tissue swelling. This information are useful before the models can be applied to the actual patient data for validation purposes.

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